Supporting Information for

Development of proneurogenic, neuroprotective small molecules

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Complete references.

Ref 19a: Pieper, A.A.; Xie, S.; Capota, E.; Estill, S.J.; Zhong, J.; Long, J.M.; Becker, G.L.; Huntington.; Goldman, S.E.; Shen, C.H.; Capota, M.; Britt, J.K.; Kotti, T.; Brat, D. J.; Williams, N.S.; MacMillan, K.S.; Naidoo, J.; Melito, L.; Hsieh, J.; De Brabander, J.; Ready, J.M.; McKnight, S.L. *Cell* **2010**, *142*, 39-51. \

Ref 38b. Drexler, D. M.; Belcastro, J. V.; Kickinson, K. E.; Edinger, K. J.; Hnatyshy, S. Y.; Josephs, J. L..; Langish, R. A.; McNaney, C. A.; Santone, K. S.; Shipkova, P. A.; Tymiak, A. A.; Zvyaga, T. A.; Sanders, M. *Assay Drug Devel. Technol.* **2007**, *5*, 247.

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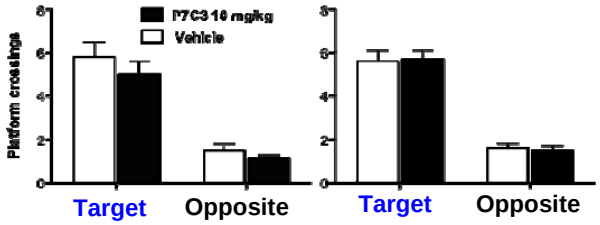
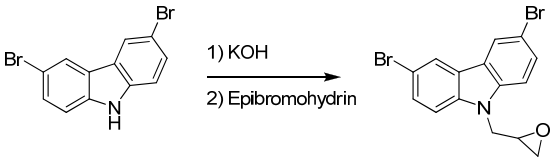


Figure S1: Daily administration of P7C3 at a known proneurogenic dose (10 mg/kg/day i.p,) to 11 month old male Fisher =-344 rats (n=18 for P7C3 and VEH control groups) for 2 months starting at 9 months of age does not improve performance in the Morris water maze task probe test, a task of hippocampal-dependent learning. This is in contrast to the ability of P7C3 to improve performance in this task following identical treatment in 20 month old aged rats, in which decline in ability to perform in this task is associated with a characteristic decline in hippocampal neurogenesis seen in these animals (ref 19, main text). These results suggest that a beneficial effect of augmenting hippocampal neurogenesis is more readily observed under conditions of pathologically diminished hippocampal neurogenesis in aged animals than under normal basal adult levels in younger adult rats.

Representative Procedure 1: Epoxide formation

3,6-Dibromo-9-(oxiran-2-ylmethyl)-9H-carbazole (Epoxide A)

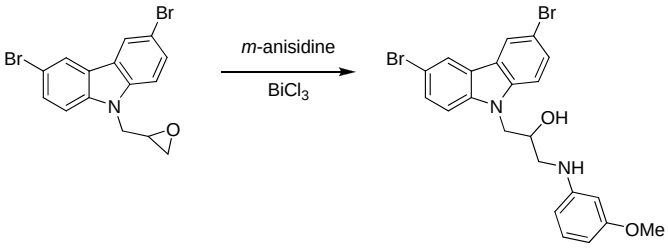


Following a literature procedure,[1] powdered KOH (0.103 g, 1.85 mmol) was added to a solution of 3,6-dibromocarbazole (0.500 g, 1.54 mmol) in DMF (1.5 mL) at ambient temperature and stirred for 30 min until dissolved. Epibromohydrin (0.32 mL, 3.8 mmol) was added via syringe and the reaction was stirred at room temperature overnight. Upon completion, the solution was partitioned between EtOAc and H_2O. The aqueous layer was washed 3×EtOAc, and the combined organics were washed with saturated aqueous NaCl, dried over Na_2SO_4, filtered, and concentrated in vacuo. The crude residue was recrystallized from EtOAc/Hexane to afford epoxide **A** (389 mg, 66%).

^{1}H NMR ($CDCl_3$, 500 MHz) δ 8.10 (d, 2H, *J* = 2.0 Hz), 7.54 (dd, 2H, *J* = 2.0, 8.5 Hz), 7.31 (d, 2H, *J* = 8.5 Hz), 4.62 (dd, 1H, *J* = 2.5, 16.0 Hz), 4.25 (dd, 1H, *J* = 5.5, 16.0 Hz), 3.29 (m, 1H), 2.79 (dd, 1H, *J* = 4.0, 4.5 Hz), 2.46 (dd, 1H, *J* = 2.5, 5.0 Hz).

Representative Procedure 2: Opening epoxide with aniline

1-(3,6-Dibromo-9H-carbazol-9-yl)-3-(3-methoxyphenylamino)propan-2-ol (7)



Following a literature procedure[ii], *m*-anisidine (1.0 mL, 8.95 mmol) was added to a suspension of epoxide **A** (3.02 g, 7.92 mmol) in cyclohexane (73 mL). $BiCl_3$ (0.657 g, 2.08 mmol) was added and the mixture was heated to reflux overnight. Upon completion, the reaction was partitioned between EtOAc and H_2O. The aqueous layer was washed 3×EtOAc, and the combined organics were washed with saturated aqueous NaCl, dried over Na_2SO_4, filtered, and concentrated in vacuo. The crude residue was purified by chromatography (SiO_2, 0–50% EtOAc/Hexane) to afford **7** as an opaque yellow solid (998 mg, 25%).

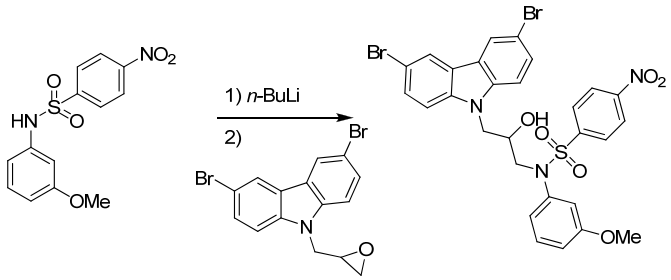
^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.12 (d, 2H, *J* = 1.6 Hz), 7.52 (dd, 2H, *J* = 2.0, 8.8 Hz), 7.32 (d, 2H, *J* = 8.8 Hz), 7.07 (t, 1H, *J* = 8.0 Hz), 6.31 (dd, 1H, *J* = 2.4, 8.0 Hz), 6.21 (dd, 1H, *J* = 2.0, 8.0 Hz), 6.12 (dd, 1H, *J* = 2.0, 2.4 Hz), 4.34–4.39 (m, 3H), 4.00 (br s, 1H), 3.71 (s, 3H), 3.30 (dd, 1H, *J* = 3.6, 13.2 Hz), 3.16 (dd, 1H, *J* = 6.4, 13.2 Hz), 2.16 (br s, 1H).

^{13}C NMR ($CDCl_3$, 100 MHz) δ 161.0, 149.2, 139.9 (2C), 130.4 (2C), 129.5 (2C), 123.8 (2C), 123.5 (2C), 112.8, 111.0 (2C), 106.7, 103.8, 99.8, 69.5, 55.3, 48.0, 47.4.

ESI *m/z*: 502.9 ($[M+H]^+$, $C_{22}H_{21}Br_2N_2O_2$ requires 503.0).

Representative Procedure 3: Epoxide opening with Ns-protected anilines

***N*-(3-(3,6-Dibromo-9H-carbazol-9-yl)-2-hydroxypropyl)-*N*-(3-methoxyphenyl)-4-nitrobenzenesulfonamide (Ns-A)**



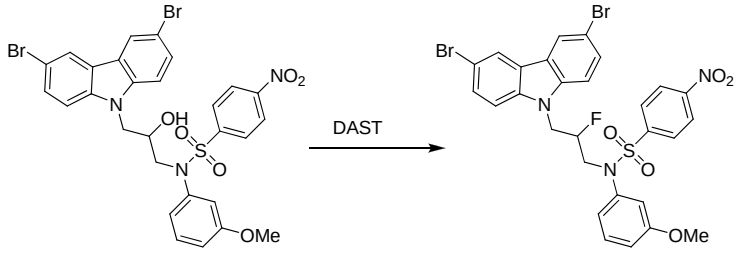
A heterogeneous mixture of *N*-(4-methoxyphenyl)-4-nitrobenzenesulfonamide (100.2 mg, 0.32 mmol) in toluene (2.5 mL, 0.13 M) under a N_2 atmosphere was cooled in a dry ice/acetone bath before dropwise addition of *n*-butyllithium (200µL of 1.78 M in hexanes, 0.36 mmol). The reaction was stirred at –78 °C for 10 minutes before addition of epoxide **A**. The heterogeneous mixture was stirred at room temperature for 5 min before heating at 100 °C for 48 h. The cooled reaction was diluted with EtOAc and washed 3×5% acetic acid solution, followed by a brine wash. The organic layer was dried over Na_2SO_4, filtered and condensed. The crude mixture was purified by chromatography (SiO_2, 100% CH_2Cl_2) to afford Ns-**A** (88%).

^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.23 (d, 2H, *J* = 8.5 Hz), 8.06 (d, 2H, *J* = 1.9 Hz), 7.65 (d, 2H, *J* = 8.5 Hz), 7.46, (dd, 2H, *J* = 1.9, 8.6 Hz), 7.22 (d, 2H, *J* = 8.8 Hz), 6.94 (d, 2H, *J* = 8.8 Hz), 6.83 (d, 2H, *J* = 9.1 Hz), 4.44 (dd, 1H, *J* = 3.6,14.9 Hz), 4.26–4.34 (m, 1H), 4.17–4.24 (br s, 1H), 3.81 (s, 3H), 3.62–3.75 (m, 2H).

ESI *m/z*: 732.0 ($[M+HCOO]^-$, $C_{29}H_{24}Br_2N_3O_8S$ requires 732.0).

Representative Procedure 4: Fluorination of P7C3 analogues

***N*-(3-(3,6-Dibromo-9H-carbazol-9-yl)-2-fluoropropyl)-*N*-(3-methoxyphenyl)-4-nitrobenzenesulfonamide (Ns-B)**



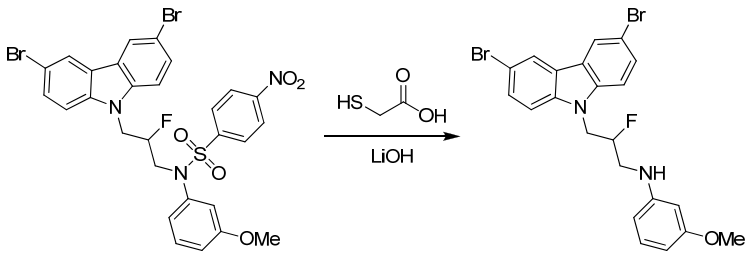
An oven dried 20 mL scintillation vial containing Ns-**A** (18.3 mg, 0.027 mmol) was purged with N_2 and charged with anhydrous CH_2Cl_2 (1.5 mL, 0.018 M). The sealed vial was cooled in a dry ice acetone bath before the dropwise addition of diethylaminosulfur trifluoride (DAST, 7 µL, 0.053 mmol). The reaction temperature was maintained at –78 °C for an hour and then slowly warmed to room temperature and stirred overnight. The reaction was quenched with 2.0 mL of saturated $NaHCO_3$ solution and diluted with 6 mL CH_2Cl_2 and extracted three times. The combined organics were dried over Na_2SO_4, filtered and condensed. The crude product was carried forward without further purification. Alternatively, morpholinosulfur trifluoride (MORPHO-DAST) can be used at r.t.

^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.28 (d, 2H, *J* = 8.0 Hz), 8.13 (s, 2H), 7.72 (d, 2H, *J* = 8.7 Hz), 7.54, (d, 2H, *J* = 8.0 Hz), 7.21 (d, 3H, *J* = 8.1 Hz), 6.89 (dd, 1H, *J* = 2.4, 8.3 Hz), 6.67 (t, 1H, *J* = 2.0 Hz), 6.55 (d, 1H, *J* = 8.0 Hz), 4.93 (m, 1H), 4.43–4.68 (m, 2H), 4.20 (t, 1H, *J* = 6.2 Hz), 3.81–3.99 (m, 2H), 3.75 (s, 3H).

ESI *m/z*: 733.9 ($[M+HCOO]^-$, $C_{29}H_{23}Br_2FN_3O_7S$ requires 734.0).

Representative Procedure 5: Nosyl group deprotection[2]

***N*-(3-(3,6-Dibromo-9H-carbazol-9-yl)-2-fluoropropyl)-3-methoxyaniline (53)**

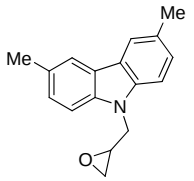


To a vial containing Ns-**B** (21.0 mg, 0.030 mmol) was added lithium hydroxide (3.2 mg, 0.134 mmol), DMF (0.5 mL, 0.06 M) and mercaptoacetic acid (4.2 µL, 0.060 mmol). After stirring at r.t. for 1 h the reaction mixture was diluted with EtOAc and washed sequentially with H_2O, saturated aqueous $NaHCO_3$, H_2O (3×) and brine. The organic layer was dried over Na_2SO_4, filtered and condensed. The crude reaction mixture was purified (SiO_2, 30% EtOAc/Hexanes + 0.2% Et_3N), to afford **53** (13.6 mg, 88%).

^{1}H NMR ($CDCl_3$, 500 MHz) δ 8.16 (d, 2H, *J* = 2.0 Hz), 7.56 (dd, 2H, *J* = 1.9, 8.7 Hz), 7.31 (d, 2H, *J* = 8.6 Hz), 7.11 (t, 1H, *J* = 8.1 Hz), 6.36 (dd, 1H, *J* = 2.2, 8.1 Hz), 6.23 (dd, 1H, *J* = 2.0, 8.0 Hz), 6.15 (t, 1H, *J* = 2.3 Hz), 5.11 (dddd, 1H, *J* = 4.6, 5.8, 10.4, 47.7 Hz), 4.60 (m, 2H), 4.39 (dm, 2H), 3.95 (t, 1H, *J* = 6.3 Hz), 3.75 (s, 3H).

ESI *m/z*: 504.9 ($[M+H]^+$, $C_{22}H_{20}Br_2FN_2O$ calculated 505.0).

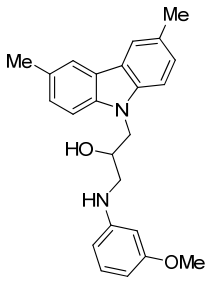
3,6-Dimethyl-9-(oxiran-2-ylmethyl)-9H-carbazole (Epoxide B)



Following Representative Procedure 1, 3,6-dimethyl carbazole[3] was added to epichlorohydrin in to afford epoxide **B** in 69% yield.

^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.84 (d, 2H, *J* = 1.0 Hz), 7.30 (d, 2H, *J* = 8.5 Hz), 7.26 (dd, 2H, *J* = 1.0, 8.5 Hz), 4.54 (dd, 1H, *J* = 3.5, 16.0 Hz), 4.35 (dd, 1H, *J* = 4.5, 16.0 Hz), 3.30 (m, 1H), 2.76 (dd, 1H, *J* = 4.0, 5.0 Hz), 2.52 (s, 6H), 2.51 (m, 1H).

1-(3,6-Dimethyl-9H-carbazol-9-yl)-3-(3-methoxyphenylamino)propan-2-ol (14)



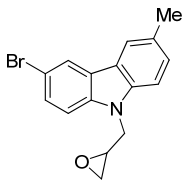
Following Representative Procedure 2, **14** was prepared from epoxide **B** in 22 % following purification by preparative TLC.

^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.84 (d, 2H, *J* = 0.5 Hz), 7.30 (d, 2H, *J* = 8.0 Hz), 7.23 (d, 2H, *J* = 8.0 Hz), 7.05 (t, 1H, *J* = 8.0 Hz), 6.28 (dd, 1H, *J* = 2.5, 8.0 Hz), 6.21 (dd, 1H, *J* = 2.5, 8.0 Hz), 6.12 (dd, 1H, *J* = 2.0, 2.5 Hz), 4.39 (m, 3H), 4.01 (br s, 1H), 3.68 (s, 3H), 3.31 (dd, 1H, *J* = 3.0, 11.5 Hz), 3.17 (dd, 1H, *J* = 6.5, 13.0 Hz), 2.51 (s, 6H), 2.13 (br s, 1H).

^{13}C NMR ($CDCl_3$, 125 MHz) δ 161.0, 149.5, 139.5 (2C), 130.3 (2C), 128.7, 127.3 (2C), 123.2 (2C), 120.5 (2C), 108.7 (2C), 106.7, 103.7, 99.5, 69.7, 55.2, 48.0, 47.4, 21.6 (2C).

ESI *m/z* 375.2 ($[M+H]^+$, $C_{24}H_{27}N_2O_2$ requires 375.2).

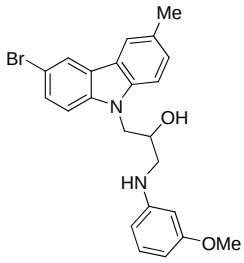
3-Bromo-6-methyl-9-(oxiran-2-ylmethyl)-9H-carbazole (Epoxide C)



Following Representative Procedure 1, epoxide **C** was prepared in 74% yield.

^{1}H NMR ($CDCl_3$, 500 MHz) δ 8.13 (d, 1H, *J* = 1.5 Hz), 7.80 (d, 1H, *J* = 1.0 Hz), 7.50 (dd, 1H, *J* = 2.0, 8.5 Hz), 7.33–7.28 (m, 3H), 4.57 (dd, 1H, *J* = 3.0, 15.5 Hz), 4.29 (dd, 1H, *J* = 5.0, 15.5 Hz), 3.29 (m, 1H), 2.77 (dd, 1H, *J* = 4.0, 4.5 Hz), 2.51 (s, 3H), 2.48 (dd, 1H, *J* = 2.5, 4.5 Hz).

1-(3-Bromo-6-methyl-9H-carbazol-9-yl)-3-(3-methoxyphenylamino)propan-2-ol (15)



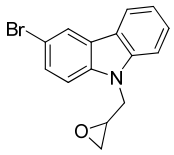
Following Representative Procedure 2, **15** was prepared from epoxide **C** in 41% yield.

^{1}H NMR ($CDCl_3$, 500 MHz) δ 8.14 (d, 1H, *J* = 2.0 Hz), 7.81 (s, 1H), 7.48 (dd, 1H, *J* = 2.0, 8.5 Hz), 7.31 (d, 1H, *J* = 5.0 Hz), 7.29 (br s, 1H), 7.06 (t, 1H, *J* = 8.5 Hz), 6.29 (dd, 1H, *J* = 2.0, 8.0 Hz), 6.21 (dd, 1H, *J* = 2.0, 8.0 Hz), 6.11 (t, 1H, *J* = 2.0 Hz), 4.37 (m, 3H), 3.99 (br s, 1H), 3.70 (s, 3H), 3.30 (dd, 1H, *J* = 3.5, 13.5 Hz), 3.16 (dd, 1H, *J* = 6.5, 13.5 Hz), 2.51 (s, 3H), 2.14 (br s, 1H).

^{13}C NMR ($CDCl_3$, 125 MHz) δ 161.0, 149.4, 139.8, 139.5, 130.3, 129.4, 128.5, 128.2, 124.7, 123.2, 122.3 120.7, 112.1, 110.6, 109.0, 106.7, 103.7, 99.6, 69.5, 55.3, 47.9, 47.4, 21.5.

ESI *m/z* 439.1 ($[M+H]^+$, $C_{23}H_{24}BrN_2O_2$ requires 439.1).

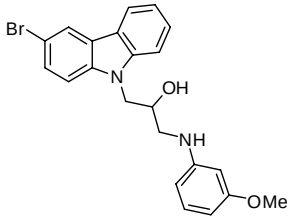
3-Bromo-9-(oxiran-2-ylmethyl)-9H-carbazole (Epoxide D)



Prepared according to Representative Procedure 1.

^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.19 (d, 1H, *J* = 1.7 Hz), 8.02 (d, 1H, *J* = 5.1 Hz), 7.58–7.42 (m, 3H), 7.35 (d, 1H, *J* = 8.7 Hz), 7.26 (t, 1H, *J* = 7.3 Hz), 4.64 (dd, 1H, *J* = 2.9, 15.9 Hz), 4.34 (dd, 1H, *J* = 4.9, 15.9 Hz), 3.33 (dt, 1H, *J* = 2.2, 5.3 Hz), 2.80 (t, 1H, *J* = 4.3 Hz), 2.52 (dd, 1H, *J* = 2.6, 4.6 Hz).

1-(3-Bromo-9H-carbazol-9-yl)-3-(3-methoxyphenylamino)propan-2-ol (16)



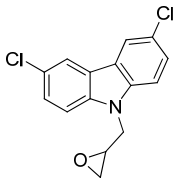
Prepared from epoxide **D** following Representative Procedure 2.

^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.21 (d, 1H, *J* = 1.9 Hz), 8.05 (d, 1H, *J* = 7.9 Hz), 7.53 (dd, 1H, *J* = 1.9, 8.7 Hz), 7.51–7.44 (m, 2H), 7.36 (d, 1H, *J* = 8.7 Hz), 7.30–7.24 (m, 1H), 7.08 (t, 1H, *J* = 8.1 Hz), 6.32 (dd, 1H, *J* = 2.3, 8.2 Hz), 6.24 (dd, 1H, *J* = 2.2, 8.0 Hz), 6.15 (t, 1H, *J* = 2.3 Hz), 4.50–4.36 (m, 3H), 4.03 (br s, 1H), 3.72 (s, 3H), 3.35 (dd, 1H, *J* = 3.2, 13.0 Hz), 3.21 (dd, 1H, *J* = 6.5, 13.0 Hz), 2.13 (d, 1H, *J* = 3.0 Hz).

^{13}C NMR ($CDCl_3$, 100 MHz) δ 161.0, 149.4, 141.2, 139.6, 130.4, 128.8, 126.9, 125.0, 123.3, 122.2, 120.8, 120.1, 112.4, 110.7, 109.4, 106.7, 103.8, 99.7, 69.6, 55.3, 48.0, 47.4.

ESI *m/z*: 425.0 ($[M + H]^+$, $C_{22}H_{22}BrN_2O_2$ requires 425.1).

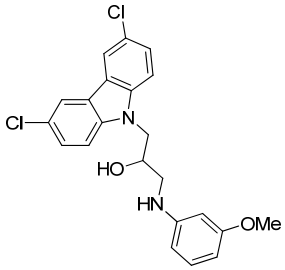
3,6-Dichloro-9-(oxiran-2-ylmethyl)-9H-carbazole (Epoxide E)



Following Representative Procedure 1, epoxide **E** was prepared in 23% yield.

^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.92 (d, 2H, *J* = 1.8 Hz), 7.40 (dd, 2H, *J* = 1.8, 9.0 Hz), 7.32 (d, 2H, *J* = 9.0 Hz), 4.59 (dd, 1H, *J* = 3.0, 16.2 Hz), 4.22 (dd, 1H, *J* = 5.4, 16.2 Hz), 3.27 (m, 1H), 2.78 (dd, 1H, *J* = 4.2, 4.8 Hz), 2.46 (dd, 1H, *J* = 2.4, 4.8 Hz).

1-(3,6-Dichloro-9H-carbazol-9-yl)-3-(3-methoxyphenylamino)propan-2-ol (17)



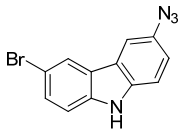
Following Representative Procedure 2, **17** was prepared from epoxide **E** in 37% yield.

^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.95 (d, 2H, *J* = 2.0 Hz), 7.38 (dd, 2H, *J* = 2.0, 8.5 Hz), 7.33 (d, 2H, *J* = 9.0 Hz), 7.06 (t, 1H, *J* = 8.0 Hz), 6.30 (dd, 1H, *J* = 2.0, 8.0 Hz), 6.20 (dd, 1H, *J* = 2.0, 8.0 Hz), 6.11 (dd, 1H, *J* = 2.0, 2.5 Hz), 4.30–4.35 (m, 3H), 3.70 (s, 3H), 3.28 (dd, 1H, *J* = 3.5, 13.0 Hz), 3.13 (dd, 1H, *J* = 6.5, 13.0 Hz).

^{13}C NMR ($CDCl_3$, 150 MHz) δ 161.0, 149.3, 139.7, 130.4 (2C), 126.9 (2C), 125.5 (2C), 123.4 (2C), 120.4 (2C), 110.5 (2C), 106.7, 103.8, 99.8, 69.6, 55.3, 48.0, 47.5.

ESI *m/z* 415.0 ($[M+H]^+$, $C_{22}H_{21}Cl_2N_2O_2$ requires 415.1).

3-Azido-6-bromo-9H-carbazole (Carbazole A)

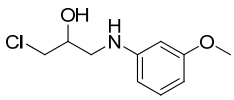


Following a literature procedure[4], 3,6-dibromocarbazole (0.500 g, 1.538 mmol), NaN_3 (0.120 g, 1.846 mmol), CuI (0.029 g, 0.154 mmol), L-proline (0.053 g, 0.461 mmol) and NaOH (0.019 g, 0.461 mmol) were dissolved in 7:3 EtOH/H_2O (3.0 mL) and heated to 95 °C under a N_2 atmosphere for 24 h. The completed reaction was partitioned between EtOAc/H_2O (3×) and the combined organics were washed with saturated aqueous NaCl, dried over Na_2SO_4, filtered, and concentrated. The crude residue was purified by flash chromatography (SiO_2, 0–15% EtOAc/toluene), followed by HPLC (Phenomenex SiO_2 Luna 10 µ, 250×21.2 mm column, 50% EtOAc/Hexane, 21 mL/min, retention time = 48 min) to afford carbazole **A**.

^{1}H NMR ($CDCl_3$, 500 MHz) δ 8.14 (s, 1H), 8.08 (br s, 1H), 7.64 (s, 1H), 7.50 (d, 1H, *J* = 8.5 Hz), 7.38 (d, 1H, *J* = 9.0 Hz), 7.29 (d, 1H, *J* = 8.5 Hz), 7.10 (d, 1H, *J* = 9.0 Hz).

ESI *m/z* 285.0 ($[M–H]^–$, $C_{12}H_6BrN_4$ requires 285.0).

1-Chloro-3-(3-methoxyphenylamino)propan-2-ol (Chlorohydrin A)

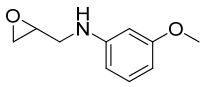


m-Anisidine (0.25 mL, 4.47 mmol) was added to epichlorohydrin (0.22 mL, 5.37 mmol) in acetic acid (0.5 mL) and the mixture was heated to 75 °C. Upon completion the reaction was neutralized with saturated $NaHCO_3$ to pH 7, then extracted 3× EtOAc, washed with brine and dried with $MgSO_4$, filtered, and concentrated in vacuo. The crude residue was purified by chromatography (SiO_2, 0–50% EtOAc/Hexane) to afford chlorohydrin **A** (303 mg, 63%).

^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.08 (t, 1H, *J* = 8.5 Hz), 6.29 (dd, 1H, *J* = 2.5, 8.5 Hz), 6.25 (dd, 1H, *J* = 2.5, 8.0 Hz), 6.19 (t, 1H, *J* = 2.5 Hz), 4.07 (m, 1H), 3.75 (s, 3H), 3.67 (dd, 1H, *J* = 4.5, 11.0 Hz), 3.62 (dd, 1H, *J* = 6.0, 11.5 Hz), 3.35 (dd, 1H, *J* = 4.5, 13.0 Hz), 3.21 (dd, 1H, *J* = 7.0, 13.0 Hz), 2.31 (br s, 1H).

ESI *m/z* 216.0 ($[M+H]^+$, $C_{10}H_{15}ClNO_2$ requires 216.1).

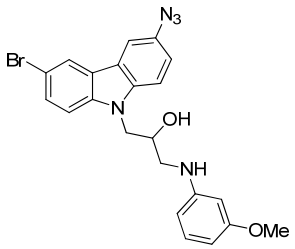
3-Methoxy-*N*-(oxiran-2-ylmethyl)aniline (Epoxide F)



Following a literature procedure[5], chlorohydrin **A** (0.300 g, 1.391 mmol) was dissolved in dioxane (4.6 mL) and KOH (0.095 g, 1.669 mmol) was added to the solution. The reaction was followed by TLC (30% EtOAc/Hexane) until the starting material was consumed and the less polar product was obtained. After aqueous workup, the crude epoxide **F** was used without purification.

^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.24 (t, 1H, *J* = 8.0 Hz), 6.28 (dd, 1H, *J* = 2.5, 8.0 Hz), 6.24 (dd, 1H, *J* = 2.0, 8.0 Hz), 6.18 (t, 1H, *J* = 2.5 Hz), 3.90 (br s, 1H), 3.76 (s, 3H), 3.51 (m, 1H), 3.22 (m, 1H), 3.18 (m, 1H), 2.80 (dd, 1H, *J* = 4.0, 4.5 Hz), 2.67 (dd, 1H, *J* = 2.0, 5.0 Hz).

1-(3-Azido-6-bromo-9H-carbazol-9-yl)-3-(3-methoxyphenylamino)propan-2-ol (18)



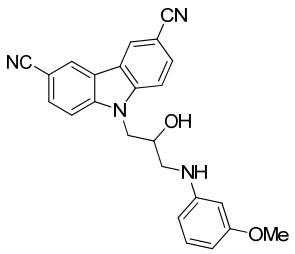
NaH (0.002 g, 0.046 mmol) was added to a solution of carbazole **A** (0.012 g, 0.042 mmol) in anhydrous THF, cooled to 0 °C and stirred for 45 min. A solution of epoxide **F** (0.009 g, 0.0502 mmol) in anhydrous THF (0.1 mL) was added dropwise to the reaction mixture. The reaction was warmed to room temperature and stirred overnight. Upon completion, the reaction was quenched with saturated aqueous NH_4Cl and extracted with EtOAc (3×). The combined organics were concentrated and purified by chromatography (SiO_2, 0–30% EtOAc/Hexane) to afford **18** (7.5 mg, 46%).

^{1}H NMR ($CDCl_3$, 500 MHz) δ 8.14 (d, 1H, *J* = 1.5 Hz), 7.64 (d, 1H, *J* = 2.0 Hz), 7.52 (dd, 1H, *J* = 1.5, 8.5 Hz), 7.40 (d, 1H, *J* = 9.0 Hz), 7.31 (d, 1H, *J* = 8.5 Hz), 7.12 (dd, 1H, *J* = 2.0, 8.5 Hz), 7.07 (dd, 1H, *J* = 8.0, 8.0 Hz), 6.31 (dd, 1H, *J* = 2.0, 8.0 Hz), 6.21 (dd, 1H, *J* = 1.5, 8.0 Hz), 6.13 (dd, 1H, *J* = 2.0, 2.5 Hz), 4.39–4.35 (m, 3H), 3.71 (s, 3H), 3.31 (dd, 1H, *J* = 3.5, 13.0 Hz), 3.16 (dd, 1H, *J* = 7.0, 13.0 Hz), 2.17 (br s, 1H).

^{13}C NMR ($CDCl_3$, 150 MHz) δ 161.1, 149.3, 140.2, 138.8, 132.4, 130.4, 129.5, 124.1, 123.6, 123.1, 118.5, 112.6, 111.0, 110.6 (2C), 106.7, 103.8, 99.8, 69.6, 55.3, 48.0, 47.5.

ESI *m/z* 466.0 ($[M+H]^+$, $C_{22}H_{21}BrN_5O_2$ requires 466.1).

9-(2-Hydroxy-3-(3-methoxyphenylamino)propyl)-9H-carbazole-3,6-dicarbonitrile (19)



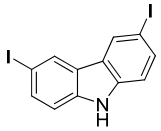
Following a literature proceudre,[6] **7** (0.0252 g, 0.05 mmol), potassium hexacyanoferrate(II) trihydrate (0.0106 g, 0.025 mmol), sodium bicarbonate (0.0106 g, 0.1 mmol) and palladium acetate (1 mol%, 0.0001 g) were combined under a N_2 atmosphere. Anhydrous dimethylacetamide (0.1 mL) was added, and the reaction mixture was stirred at 120 °C overnight. The crude reaction mixture was diluted with 10 mL EtOAc and washed with H_2O (2×10 mL) and brine (1×30 mL). The organic layer was dried over anhydrous Na_2SO_4 and evaporated to afford the crude product, which was purified by chromatography (SiO_2, Hexanes/EtOAc) to afford **19** as a white solid (0.0110 g, 55%).

^{1}H NMR (acetone-d_6, 400 MHz) δ 8.74 (s, 2H), 7.91 (d, 2H, *J* = 8.6 Hz), 7.84 (dd, 2H, *J* = 1.2, 8.6 Hz), 7.01 (t, 1H, *J* = 8.1 Hz), 6.31 (dd, 1H, *J* = 1.2, 8.1 Hz), 6.27 (t, 1H, *J* = 2.0 Hz), 6.22 (dd, 1H, *J* = 2.1, 8.1 Hz), 5.16 (t, 1H, *J* = 5.8 Hz), 4.77 (dd, 1H, *J* = 3.4, 15.1 Hz), 4.66 (dd, 1H, *J* = 8.5, 15.0 Hz), 4.44 (br s, 1H), 3.71 (s, 3H), 3.50–3.43 (m, 1H), 3.36–3.28 (m, 1H), 2.81 (s, 1H).

^{13}C NMR (acetone-d_6, 125 MHz) δ 161.3, 150.4, 143.9, 130.02, 129.95, 126.0, 122.4, 119.8, 112.0, 106.0, 103.3, 102.5, 98.9, 69.0, 54.5, 48.0, 47.7.

ESI *m/z* 441.1 ($[M + HCOO]^-$, $C_{25}H_{21}N_4O_4$ requires 441.2).

3,6-Diiodo-9H-carbazole (Carbazole B)

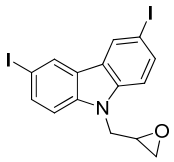


Following a literature procedure[7], to a solution of 9H-carbazole (0.0500 g, 0.299 mmol) and bis(pyridine)iodine(I) tetrafluoroborate (0.2780 g, 0.748 mmol) in 8 mL CH_2Cl_2, was added dropwise trifluoromethanesulfonic acid (26.5 µL, 0.299 mmol). The mixture was sealed and stirred in a 20 mL scintillation vial at room temperature for 20 h or until TLC showed the complete disappearance of starting material. The crude was diluted with 30 mL EtOAc and washed 3×30 mL with saturated $NaHCO_3$ and 1×30 mL with brine. The organic layer was dried over anhydrous Na_2SO_4 and evaporated to afford the crude product, which was purified by chromatography (SiO_2, Hexanes/EtOAc) to afford carbazole **B** as a white solid (0.0212 g, yield 21%).

^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.33 (d, 1H, *J* = 1.0 Hz), 8.10 (br s, 1H), 7.68 (dd, 1H, *J* = 1.7, 8.5 Hz), 7.22 (d, 1H, *J* = 8.5 Hz).

ESI *m/z* 417.8 ($[M–H]^-$, $C_{12}H_6I_2N$ requires 417.9).

3,6-Diiodo-9-(oxiran-2-ylmethyl)-9H-carbazole (Epoxide G)

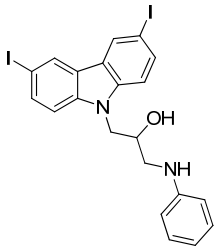


Following Representative Procedure 1, epoxide **G** was prepared from carbazole **B** in 96% yield.

^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.33 (d, 2H, *J* = 1.7 Hz), 7.73 (dd, 2H, *J* = 1.6, 8.6 Hz), 7.24 (d, 2H, *J* = 8.6 Hz), 4.64 (dd, 1H, *J* = 2.7, 15.9 Hz), 4.28 (dd, 1H, *J* = 5.1, 16.0 Hz), 3.37–3.24 (m, 1H), 2.80 (t, 1H, *J* = 4.3 Hz), 2.48 (dd, 1H, *J* = 2.6, 4.6 Hz).

^{13}C NMR ($CDCl_3$, 125 MHz) δ 140.0, 135.0, 129.5, 124.3, 111.3, 82.6, 50.6, 45.2, 44.9.

1-(3,6-Diiodo-9H-carbazol-9-yl)-3-(phenylamino)propan-2-ol (20)



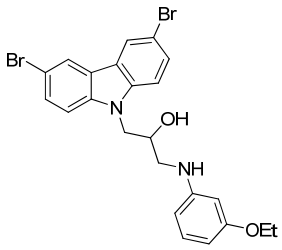
Following Representative Procedure 2, **20** was prepared from epoxide **G** in 28% yield.

^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.35 (s, 2H), 7.72 (d, 2H, *J* = 8.6 Hz), 7.28 (d, 2H, *J* = 2.5 Hz), 7.20 (t, 2H, *J* = 7.7 Hz), 6.78 (t, 1H, *J* = 7.3 Hz), 6.63 (d, 2H, *J* = 8.3 Hz), 4.49–4.29 (m, 3H), 3.33 (d, 1H, *J* = 10.9 Hz), 3.19 (dd, 1H, *J* = 6.1, 12.8 Hz), 2.92 (br s, 1H).

^{13}C NMR ($CDCl_3$, 100 MHz) δ 147.9, 140.1, 135.1, 129.65, 129.63, 124.4, 118.9, 113.7, 111.5, 82.6, 69.6, 48.0, 47.3.

ESI *m/z* 613.0 ($[M+HCOO]^-$, $C_{22}H_{19}I_2N_2O_3$ requires 613.0).

1-(3,6-Dibromo-9H-carbazol-9-yl)-3-(3-ethoxyphenylamino)propan-2-ol (21)



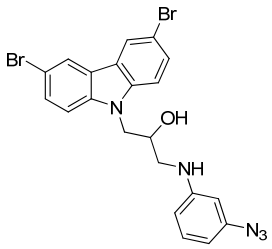
Following Representative Procedure 2, **21** was prepared from epoxide **A** in 53% yield.

^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.13 (d, 2H, *J* = 1.9 Hz), 7.53 (dd, 2H, *J* = 1.9, 8.7 Hz), 7.32 (d, 2H, *J* = 8.7 Hz), 7.04 (t, 1H, *J* = 8.1 Hz), 6.20 (d, 1H, *J* = 9.6 Hz), 6.12 (d, 1H, *J* = 2.2 Hz), 4.49–4.36 (m, 3H), 4.05–3.91 (m, 3H), 3.29 (d, 1H, *J* = 12.2 Hz), 3.18 (d, 1H, *J* = 16.0 Hz), 2.12 (d, 1H, *J* = 3.2 Hz), 1.36 (t, 3H, *J* = 7.0 Hz).

^{13}C NMR ($CDCl_3$, 100 MHz) δ 160.4, 149.2, 139.9 (2C), 130.4 (2C), 129.5 (2C), 123.8, 123.5 (2C), 112.8 (2C), 111.0 (2C), 106.7, 104.4, 100.2, 69.5, 63.4, 48.0, 47.4, 15.1.

ESI *m/z* 516.9 $([M+H])^+$, $C_{23}H_{23}Br_2N_2O_2$ requires 517.0).

1-(3-Azidophenylamino)-3-(3,6-dibromo-9H-carbazol-9-yl)propan-2-ol (22)



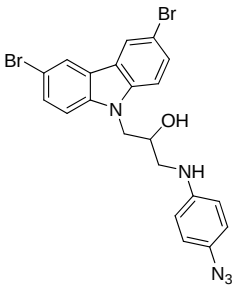
Following Representative Procedure 2, **22** was prepared from epoxide **A** in 14% yield.

^{1}H NMR ($CDCl_3$, 500 MHz) δ 8.13 (d, 2H, *J* = 2.0 Hz), 7.53 (dd, 2H, *J* = 2.0, 8.5 Hz), 7.31 (d, 2H, *J* = 8.5 Hz), 7.12 (t, 1H, *J* = 8.0 Hz), 6.44 (dd, 1H, *J* = 1.5, 8.0 Hz), 6.36 (dd, 1H, *J* = 1.5, 8.0 Hz), 6.20 (dd, 1H, *J* = 2.0 Hz), 4.35–4.41 (m, 3H), 4.10 (br s, 1H), 3.31 (dd, 1H, *J* = 3.0, 13.0 Hz), 3.17 (dd, 1H, *J* = 6.5, 13.0 Hz), 2.11 (br s, 1H).

^{13}C NMR ($CDCl_3$, 100 MHz) δ 149.3, 141.4, 139.8 (2C), 130.4, 130.3, 129.6 (2C), 123.9 (2C), 123.6 (2C), 112.9 (2C), 110.9, 109.1, 69.5, 47.6, 47.4.

ESI *m/z* 513.9 ($[M+H]^+$, $C_{21}H_{18}Br_2N_5O$ requires 514.0).

1-(4-Azidophenylamino)-3-(3,6-dibromo-9H-carbazol-9-yl)propan-2-ol (23)



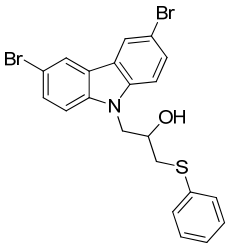
Following Representative Procedure 2, **23** was prepared from epoxide **A** in 23% yield.

^{1}H NMR (acetone-d_6, 500 MHz) δ 8.36 (d, 2H, *J* = 2.0 Hz), 7.61 (m, 2H), 7.55 (m, 2H), 6.85 (m, 2H), 6.74 (m, 2H), 5.19 (br s, 1H), 4.61 (dd, 1H, *J* = 4.0, 15.0 Hz), 4.56 (br s, 1H), 4.50 (dd, 1H, *J* = 8.0, 15.0 Hz), 4.39 (m, 1H), 3.39 (dd, 1H, *J* = 4.5, 13.0 Hz), 3.25 (dd, 1H, *J* = 6.5, 13.0 Hz).

^{13}C NMR (acetone-d_6, 100 MHz) δ 147.7, 141.1, 129.8 (2C), 128.9, 124.5, 124.0 (2C), 120.7 (2C), 114.9 (2C), 112.8 (2C), 112.6, 111.9, 69.6, 48.5, 48.4.

ESI *m/z* 513.9 ($[M+H]^+$, $C_{21}H_{18}Br_2N_5O$ requires 514.0).

1-(3,6-Dibromo-9H-carbazol-9-yl)-3-(phenylthio)propan-2-ol (24)



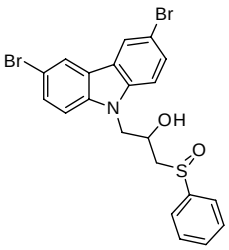
Benzenethiol (30 μL, 0.29 mmol) was added to a solution of epoxide **A** (101.6 mg, 0.27 mmol) in 5.0 mL MeOH at r.t. The reaction mixture was heated to 80 °C and stirred overnight at the same temperature. The reaction was monitored by LC/MS for the consumption of SM. The reaction was cooled, diluted with EtOAc and washed with H_2O and brine. The organic layer was dried over Na_2SO_4, filtered and condensed.

^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.03 (d, 2H, *J* = 2.1 Hz), 7.48 (dd, 2H, *J* = 2.0, 8.7 Hz), 7.33–7.20 (m, 7H), 4.33 (dd, 1H, *J* = 4.3, 14.9 Hz), 4.20 (dd, 1H, *J* = 6.9, 14.9 Hz), 4.00–4.12 (m, 1H), 3.05 (dd, 1H, *J* = 5.3, 13.9 Hz), 2.93 (dd, 1H, *J* = 7.2, 13.9 Hz), 2.51 (br s, 1H).

^{13}C NMR ($CDCl_3$, 126 MHz) δ 139.9, 134.5, 130.4, 129.6, 129.4, 127.4, 123.8, 123.4, 112.7, 111.1, 69.3, 48.1, 39.4.

ESI *m/z*: 523.9 ($[M+Cl]^-$; $C_{21}H_{17}Br_2ClNOS$ requires 523.9); 533.9 ($[M+HCOO]^-$ $C_{22}H_{18}Br_2NO_3S$ requires 533.9).

1-(3,6-Dibromo-9H-carbazol-9-yl)-3-(phenylsulfinyl)propan-2-ol (25)



An aqueous solution of $NaIO_4$ (5.14 g) was added to silica gel (20 g) and shaken until a free-flowing solid was obtained. A mixture of **24** (0.0120 g, 0.0244 mmol) and $NaIO_4$/silica gel (0.1018 g $NaIO_4$, 0.122 mmol) were suspended in CH_2Cl_2 (1 mL). The white suspension was heated to 50 °C in a sealed vial for 4 h until TLC showed complete disappearance of starting material. The reaction mixture was subjected to chromatography (SiO_2, 1:9 Hexanes/EtOAc) to afford **25** as a white solid (0.0081 g, 65%, as a 1:1 mixture of diastereomers).

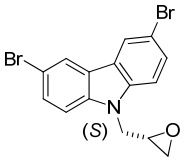
^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.13 (d, 2H, *J* = 1.9 Hz, Diast. B), 8.08 (d, 2H, *J* = 1.9 Hz, Diast. A), 7.60–7.30 (m, 7H Diast. A + 7H Diast. B), 7.34 (d, 2H, *J* = 8.8 Hz, Diast. B), 7.16 (d, 2H, *J* = 8.7 Hz, Diast. A), 4.87–4.76

(m, 1H, Diast. B), 4.65–4.55 (m, 1H, Diast. A), 4.45 (dd, 1H, *J* = 6.4, 15.1 Hz, Diast. B), 4.35 (dd, 1H, *J* = 6.0, 15.2 Hz, Diast. B), 4.30 (dd, 1H, *J* = 6.7, 15.2 Hz, Diast. B), 4.24 (dd, 1H, *J* = 6.3, 15.0 Hz, Diast. A), 3.96 (d, 1H, *J* = 2.6 Hz, Diast. A), 3.90 (d, 1H, *J* = 1.7 Hz, Diast. B), 3.15 (dd, 1H, *J* = 9.3, 13.7 Hz, Diast. A), 2.97 (dd, 1H, *J* = 8.6, 13.2 Hz, Diast. B), 2.83 (dd, 1H, *J* = 2.9, 13.2 Hz, Diast. B), 2.39 (dd, 1H, *J* = 1.7, 13.7 Hz, Diast. A).

^{13}C NMR ($CDCl_3$, 125 MHz) δ 176.3, 175.2, 171.0, 170.8, 162.2, 162.1, 160.65, 160.56, 160.0, 155.4, 155.0, 154.6, 154.5, 154.33, 154.26, 143.46, 143.45, 142.64, 142.61, 96.5, 95.5, 93.5, 91.4, 79.88, 79.87.

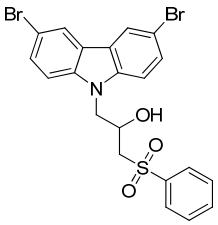
ESI *m/z*: 549.9 ($[M + HCOO]^-$ $C_{22}H_{18}Br_2NO_4S$ requires 549.9).

(*S*)-3,6-Dibromo-9-(oxiran-2-ylmethyl)-9H-carbazole ((*S*)-epoxide A)



To a solution of 3,6-dibromocarbazole (0.2194 g, 0.675 mmol) and triphenylphosphine (0.1770 g, 0.675 mmol) in THF (5.4 mL) was added *S*-(–)-glycidol (44.8 μL, 0.0500 g, 0.675 mmol). The reaction mixture was cooled in an ice bath and diethyl azodicarboxylate (106.3 μL, 0.1175 g, 0.675 mmol) was added. The reaction mixture was allowed to warm to room temperature and stir overnight. THF was removed under vacuum and the residue was dissolved in 30 mL EtOAc and washed with brine (3×30 mL). The organic layer was dried over anhydrous Na_2SO_4 and evaporated to afford the crude product, which was subjected to silica gel chromatography using Hexanes/EtOAc to afford white solid as product (0.0514 g, yield 20.0%).

1-(3,6-Dibromo-9H-carbazol-9-yl)-3-(phenylsulfonyl)propan-2-ol (26)



To a solution of **24** (0.0113 g, 0.0230 mmol) in 0.5 mL CH_2Cl_2, a solution of *m*CPBA (ca. 77% pure, 0.0129 g, 0.0575 mmol) in 0.5 mL CH_2Cl_2 was added dropwise. The mixture was stirred at room temperature overnight. The crude reaction mixture was neutralized by 9 mL Et_3N and stirred for 30 min, then diluted with 30 mL EtOAc and washed with saturated $NaHCO_3$ 3×30 mL and brine 1×30 mL. The organic layer was dried over anhydrous Na_2SO_4 and evaporated to afford the crude product, which was purified by chromatography (SiO_2, 30% EtOAc/Hexanes) to afford **26** as a white solid (0.0120 g, 99.7%).

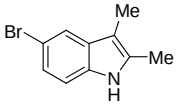
^{1}H NMR ($CDCl_3$, 400 MHz**)** δ 8.11 (d, 2H, *J* = 1.9 Hz), 7.79 (dd, 2H, *J* = 1.2, 8.4 Hz), 7.60–7.70 (m, 1H), 7.47–7.56 (m, 4H), 7.25–7.31 (m, 2H), 4.60–4.76 (m, 1H), 4.38 (d, 2H, *J* = 6.3 Hz), 3.21–3.31 (m, 2H), 3.15 (dd, 1H, *J* = 3.0, 14.2 Hz).

^{13}C NMR ($CDCl_3$, 100 MHz) δ 139.7, 138.7, 134.6, 129.8, 129.7, 128.0, 123.9, 123.5, 113.1, 110.9, 65.8, 60.0, 48.4.

ESI *m/z*: 565.9 ($[M + HCOO]^-$, $C_{22}H_{18}Br_2NO_5S$ requires 565.9); 543.7 ($[M + Na]^+$, $C_{21}H_{17}Br_2NNaO_3S$ requires 543.9).

Optically active versions of **26** were prepared from (*R*)- or (*S*)-epoxide **A** using the same procedures described for **24** and **26**.

5-Bromo-2,3-dimethyl-1H-indole (Indole A)



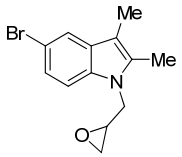
Following a published procedure,[8] 2-butanone (0.11 mL, 1.278 mmol) was added to a solution of 4-bromophenylhydrazine hydrochloride (0.300 g, 1.342 mmol) in EtOH (3.8 mL). The mixture was heated to reflux for 22 h, concentrated in vacuo, and partitioned between EtOAc and 1N HCl. The organic layer was washed with H_2O and saturated aqueous $NaHCO_3$, dried over Na_2SO_4, filtered, and

concentrated. The crude residue was purified by chromatography (SiO_2, 0–20% EtOAc/Hexane) to afford indole **A** as a pink powder (200 mg, 67%).

^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.69 (br s, 1H), 7.55 (d, 1H, *J* = 2.0 Hz), 7.15 (dd, 1H, *J* = 2.0, 8.5 Hz), 7.09 (dd, 1H, *J* = 0.5, 8.5 Hz), 2.34 (s, 3H), 2.15 (d, 3H, *J* = 0.5 Hz).

ESI *m/z* 224.0 ($[M+H]^+$, $C_{10}H_{11}BrN$ requires 224.0).

5-Bromo-2,3-dimethyl-1-(oxiran-2-ylmethyl)-1H-indole (Epoxide H)

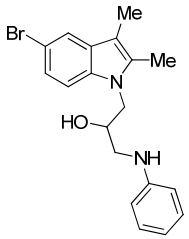


Following Representative Procedure 1, epoxide **H** was prepared from indole **A** in 48% yield.

^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.58 (d, 1H, *J* = 2.0 Hz), 7.20 (dd, 1H, *J* = 2.0, 8.5 Hz), 7.10 (d, 1H, *J* = 8.5 Hz), 4.35 (dd, 1H, *J* = 3.0, 16.0 Hz), 4.09 (dd, 1H, *J* = 4.5, 16.0 Hz), 3.17 (m, 1H), 2.72 (t, 1H, *J* = 4.5 Hz), 2.35 (dd, 1H, *J* = 3.0, 5.0 Hz), 2.33 (s, 3H), 2.19 (s, 3H).

ESI *m/z* 280.0 ($[M+H]^+$, $C_{13}H_{15}BrNO$ requires 280.0).

1-(5-Bromo-2,3-dimethyl-1H-indol-1-yl)-3-(phenylamino)propan-2-ol (27)



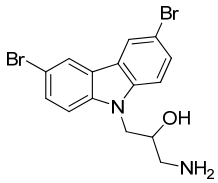
Following Representative Procedure 2, **27** was prepared from epoxide **H** in 39% yield.

^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.58 (d, 1H, *J* = 2.0 Hz), 7.17 (dd, 2H, *J* = 7.0, 8.5 Hz), 7.11 (d, 1H, *J* = 8.5 Hz), 6.75 (t, 1H, *J* = 7.0 Hz), 6.60 (d, 2H, *J* = 8.5 Hz), 4.17 (m, 1H), 4.15 (m, 2H), 3.27 (dd, 1H, *J* = 3.0, 8.5 Hz), 3.12 (dd, 1H, *J* = 7.0, 13.0 Hz), 2.34 (s, 3H), 2.19 (s, 3H).

^{13}C NMR ($CDCl_3$, 125 MHz) δ 147.9, 135.1, 134.3, 130.6, 129.6 (2C), 123.6, 120.9, 118.6, 113.7 (2C), 112.5, 110.5, 107.1, 69.9, 47.7, 47.4, 10.7, 9.0.

ESI *m/z* 373.0 ($[M+H]^+$, $C_{19}H_{22}BrN_2O$ requires 373.1).

1-Amino-3-(3,6-dibromo-9H-carbazol-9-yl)propan-2-ol (28)



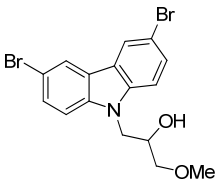
Following a published procedure[9], epoxide **A** (500mg, 1.3 mmol) was added to a 25 mL scintillation vial followed by NH_3-MeOH (2M, 6.6 mL, 13.12 mmol). The vial was heated to reflux for 24 h. Upon completion the reaction was cooled to room temperature and concentrated under reduced pressure to remove the remaining methanol. The crude residue was purified by chromatography (SiO_2, 0–10% MeOH/CH_2Cl_2) to afford **28** as an amorphous yellow foam.

^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.10 (d, 2H, *J* = 1.8 Hz), 7.52 (dd, 2H, *J* = 1.6, 8.7 Hz), 7.31 (d, 2H, *J* = 8.7 Hz), 4.25 (d, 2H, *J* = 4.7 Hz), 3.97 (br s, 1H), 2.83 (br s, 1H), 2.56 (s, 1H), 2.0 (br s, 3H).

^{13}C NMR (acetone-d_6, 100 MHz) δ 141.0 (2C), 129.7 (2C), 124.4 (2C), 124.0 (2C), 113.0 (2C), 112.5 (2C), 76.3, 50.0, 48.0.

ESI *m/z* 396.9 ([M+H]$^+$, $C_{15}H_{15}Br_2N_2O$ requires 397.0).

1-(3,6-Dibromo-9H-carbazol-9-yl)-3-methoxypropan-2-ol (29)



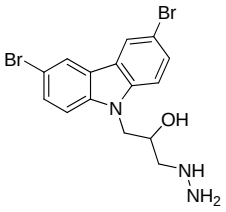
Following a published procedure[10], epoxide **A** (100 mg, 0.262 mmol) and NaOMe (14 mg, 0.262 mmol) were added to a 25 mL scintillation vial followed by the addition of MeOH (1 mL). The reaction was heated to reflux for 1 h. Upon completion, the reaction was cooled to room temperature and concentrated under reduced pressure. The crude residue was purified by chromatography (SiO_2, 0–50% EtOAc/Hexane) to afford **29** as a white solid (53 mg, 54%).

^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.14 (d, 2H, *J* = 1.8), 7.56 (dd, 2H, *J* = 1.9, 8.7 Hz), 7.36 (d, 2H, *J* = 1.9, 8.7 Hz), 4.42 (dd, 1H, *J* = 6.7, 15.0 Hz), 4.33 (dd, 1H, *J* = 5.9, 15.0 Hz), 4.20 (m, 1H), 3.41 (dd, 1H, *J* = 4.0, 9.6 Hz), 3.37 (s, 3H), 3.22 (dd, 1H, *J* = 4.8, 9.6 Hz), 2.37 (d, 1H, *J* = 6.1 Hz).

^{13}C NMR ($CDCl_3$, 100 MHz) δ 139.8 (2C), 129.4 (2C), 123.7 (2C), 123.4 (2C), 112.6 (2C), 110.9 (2C), 73.4, 69.3, 59.3, 45.8.

ESI *m/z* 411.9 ([M+H])$^+$, $C_{16}H_{16}Br_2NO_2$ requires 412.0).

1-(3,6-Dibromo-9H-carbazol-9-yl)-3-hydrazinylpropan-2-ol (30)

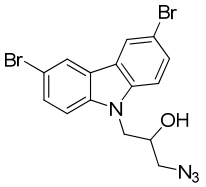


Following a literature procedure[11], epoxide **A** (100 mg, 0.262 mmol) was added to 10 mL of hydrazine hydrate and heated to 100 °C for 1 h. Upon completion, the reaction was cooled to room temperature and concentrated in vacuo. The material was partitioned between EtOAc and H_2O. The aqueous layer was washed 3×EtOAc. The organic extract was combined and washed with brine, dried over Na_2SO_4, filtered, and concentrated in vacuo. The crude material was used without further purification.

^{1}H NMR ($CDCl_3$, 400 MHz,) δ 8.12 (d, 2H, *J* = 1.9 Hz), 7.51 (dd, 2H, *J* = 1.9, 8.7 Hz), 7.43 (d, 2H, *J* = 8.7 Hz), 4.47 (dd, 1H, *J* = 8.2, 17.4 Hz), 4.41–4.23 (m, 3H), 3.23 (m, 1H), 1.95 (s, 3H), 1.75 (s, 1H).

ESI *m/z* 411.9 ([M+H]$^+$, $C_{13}H_{16}Br_2N_3O$ requires 412.0).

1-Azido-3-(3,6-dibromo-9H-carbazol-9-yl)propan-2-ol (31)

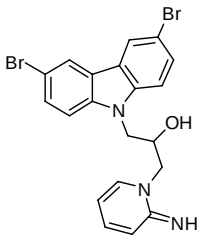


Following a literature procedure[xi], epoxide **A** (100 mg, 0.262 mmol) was added to a 25 mL scintillation vial , followed by the addition of NaN_3 (22 mg, 0.34 mmol), NH_4Cl (18 mg, 0.34 mmol) in 800 µL of EtOH and 200 µL of H_2O and heated to 80 °C overnight. Upon completion the reaction was cooled to room temperature and concentrated under reduced pressure. The crude mixture was partitioned between H_2O and EtOAc, and then washed 3×H_2O, brine, dried over $MgSO_4$, and concentrated in vacuo. The crude material was used without further purification.

^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.13 (s, 2H), 7.56 (dd, 2H, *J* = 1.9, 8.7 Hz), 7.39–7.28 (m, 2H), 4.34 (d, 2H, *J* = 6.1 Hz), 4.24 (d, 1H, *J* = 5.1 Hz), 3.48 (dd, 1H, *J* = 4.3, 12.5 Hz), 3.33 (dd, 1H, *J* = 5.6, 12.5 Hz), 2.10 (s, 1H).

ESI *m/z* 422.9 ($[M+H]^+$, $C_{15}H_{13}Br_2N_4O$ requires 423.0).

1-(3,6-Dibromo-9H-carbazol-9-yl)-3-(2-iminopyridin-1(2H)-yl)propan-2-ol (32)



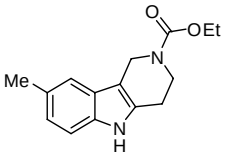
Following Representative Procedure 2, **32** was prepared from epoxide **A**, but using a reaction time of 2 d at 80 °C. The crude product was used without further purification.

^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.14 (2H, *J* = 1.9 Hz), 7.55 (dd, 2H, *J* = 1.9, 8.8 Hz), 7.35 (d, 2H, *J* = 8.7 Hz), 6.83 (t, 1H, *J* = 7.6 Hz), 6.37 (d, 1H, *J* = 6.8 Hz), 6.32 (d, 1H, *J* = 9.1 Hz) , 5.65 (t, 1H, *J* = 6.7 Hz), 4.39 (dm, 5H), 3.54 (d, 1H, *J* = 13.9 Hz).

^{13}C NMR (d_6-DMSO, 126 MHz) δ□159.8, 139.8, 139.6, 134.9, 128.7, 123.2, 123.0, 119.8, 112.3, 111.3, 102.5, 68.4, 55.7, 47.5.

ESI *m/z* 473.9 ($[M+H]^+$, $C_{20}H_{18}Br_2N_3O$ requires 474.0).

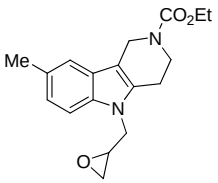
Ethyl 8-Methyl-3,4-dihydro-1H-pyrido[4,3-b]indole-2(5H)-carboxylate (Carboline A)



Following a literature procedure[12], *p*-tolylhydrazine hydrochloride (0.500 g, 3.15 mmol) and 1-carbethoxy-4-piperidone (0.18 mL, 1.17 mmol) were suspended in EtOH (0.880 mL) and heated to reflux for 2 h. The reaction mixture was removed from heat and allowed to stand overnight at ambient temperature. The resulting mixture was filtered and washed with 50% aqueous EtOH to afford carboline **A** as a beige powder (259 mg, 86%).

^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.73 (br s, 1H), 7.23 (s, 1H), 7.18 (d, 1H, *J* = 8.0 Hz), 6.96 (d, 1H, *J* = 8.0 Hz), 4.64 (br s, 2H), 4.18 (q, 2H, *J* = 7.0 Hz), 3.85 (m, 2H), 2.81 (br s, 2H), 2.42 (s, 3H), 1.28 (t, 3H, *J* = 7.0 Hz).

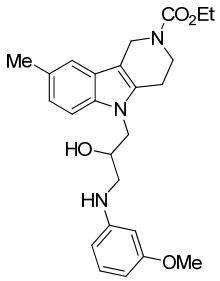
Ethyl 8-Methyl-5-(oxiran-2-ylmethyl)-3,4-dihydro-1H-pyrido[4,3-*b*]indole-2(5H)-carboxylate (Epoxide I)



Carboline **A** (0.025 g, 0.097 mmol) was dissolved in anhydrous degassed THF and was cooled to –78 °C. A solution of *n*-BuLi (0.082 mL, 1.78 M in hexanes) was added dropwise and the reaction was stirred at –78 °C for 30 min. Epibromohydrin (0.016 mL, 0.194 mmol) was added and the reaction was allowed to warm slowly to ambient temperature. After 3.5 h, epibromohydrin (0.008 mL, 0.097 mmol) was added and the reaction was stirred overnight at ambient temperature. Upon completion, the reaction was quenched with saturated aqueous NH_4Cl and the mixture was extracted with EtOAc (3×). The combined organic layers were washed with brine, dried over Na_2SO_4, filtered, and concentrated. The crude residue was purified by chromatography (SiO_2, 0–50% EtOAc/Hexane) to afford epoxide **I** (15 mg, 49%).

^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.19 (m, 1H), 7.00 (d, 1H, *J* = 8.5 Hz), 4.65 (br s, 2H), 4.32 (dd, 1H, *J* = 3.0, 15.5 Hz), 4.18 (q, 2H, *J* = 7.0 Hz), 4.08 (dd, 1H, *J* = 5.0, 15.5 Hz), 3.85 (m, 2H), 3.18 (m, 1H), 2.81 (br s, 2H), 2.73 (dd, 1H, *J* = 4.0, 4.5 Hz), 2.44 (s, 3H), 2.38 (br s, 1H), 1.29 (t, 3H, *J* = 7.0 Hz).

Ethyl 5-(2-Hydroxy-3-(3-methoxyphenylamino)propyl)-8-methyl-3,4-dihydro-1H-pyrido[4,3-*b*]indole-2(5H)-carboxylate (33)

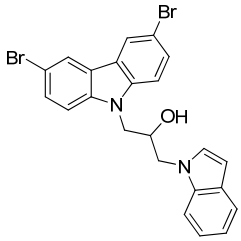


Following a literature procedure[13], LiBr (0.001 g, 0.010 mmol) and *m*-anisidine (0.011 mL, 0.102 mmol) were added to epoxide **I** (0.032 g, 0.102 mmol) and stirred vigorously at ambient temperature overnight. Upon completion the reaction was partitioned between EtOAc/H_2O, and the organic layer was concentrated to an orange oil. The crude residue was purified by chromatography (SiO_2, 0–50% EtOAc/Hexane) to afford **33** (30 mg, 67%).

^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.23 (br s, 1H), 7.17 (d, 1H, *J* = 8.0 Hz), 7.05 (dd, 1H, *J* = 8.0 Hz), 6.97 (d, 1H, *J* = 8.5 Hz), 6.28 (dd, 1H, *J* = 1.5, 8.0 Hz), 6.19 (d, 1H, *J* = 8.0 Hz), 6.11 (br s, 1H), 4.64 (br s, 2H), 4.18 (m, 1H), 4.16 (q, 2H, *J* = 7.5 Hz), 4.12 (m, 1H), 3.80 (br s, 2H), 3.71 (s, 3H), 3.23 (dd, 1H, *J* = 3.5, 13.0 Hz), 3.07 (dd, 1H, *J* = 7.5, 13.0 Hz), 2.83 (m, 1H), 2.76 (m, 1H), 2.42 (s, 3H), 1.27 (t, 3H, *J* = 7.0 Hz).

ESI *m/z* 438.2 ($[M+H]^+$, $C_{25}H_{32}N_3O_4$ requires 438.2).

1-(3,6-Dibromo-9H-carbazol-9-yl)-3-(1H-indol-1-yl)propan-2-ol (34)



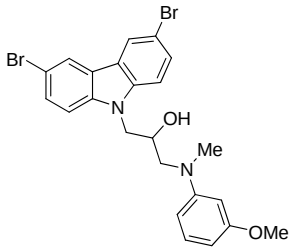
Following a literature procedure[14], indole (28 mg, 2.36 mmol) was added to a suspension of NaH (7 mg, 2.75 mmol) in 1 mL DMF at 0 °C. The mixture was allowed to stir at 0 °C for 10 min and then ambient temperature for 30 min. A solution of epoxide **A** (75 mg, 0.2 mmol) in 4 mL of DMF was added and the reaction mixture was heated to 60 °C for 3 h. Upon completion, the reaction was cooled to room temperature and partitioned between diethyl ether and H_2O. The aqueous layer was washed 3× Et_2O. The organic extracts were combined and washed with brine, dried over Na_2SO_4, filtered, and concentrated in vacuo. The crude residue was purified by chromatography (SiO_2, 0–50% EtOAc/Hexane) to afford the desired alcohol as a white foam (53 mg, 54%).

^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.12 (d, 2H, *J* = 1.9 Hz),7.64 (d, 1H, *J* = 7.8 Hz), 7.50 (dd, 2H, *J* = 1.9, 8.7), 7.23–7.08 (m, 6H), 6.55 (d, 1H, *J* = 3.2 Hz), 4.57–4.47 (m, 1H), 4.36–4.19 (m, 4H), 1.89 (d, 1H, *J* = 3.8 Hz).

^{13}C NMR ($CDCl_3$, 100 MHz) δ 139.7 (2C), 136.3, 129.5 (2C), 128.9, 128.4, 123.8 (2C), 123.5 (2C), 122.3, 121.6, 120.1 112.8 (2C), 110.8 (2C), 109.3, 102.6, 70.5, 50.3, 47.2.

ESI *m/z* 496.9 $([M+H])^+$, $C_{23}H_{19}Br_2N_2O_2$ requires 497.0).

1-(3,6-Dibromo-9H-carbazol-9-yl)-3-((3-methoxyphenyl)(methyl)amino)propan-2-ol (35)



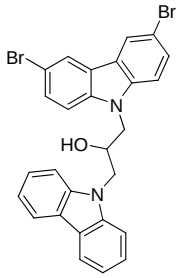
Following Representative Procedure 2, **35** was prepared from epoxide **A** in 60% yield.

^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.12 (d, 2H, *J* = 1.9 Hz), 7.53 (dd, 2H, *J* = 1.9, 8.7 Hz), 7.30 (d, 2H, *J* = 8.7 Hz), 7.11 (t, 1H, *J* = 8.2 Hz), 6.36–6.29 (m, 2H), 6.23 (t, 1H, *J* = 2.3 Hz), 4.39 (s, 1H), 4.37–4.31 (m, 2H), 3.68 (s, 3H), 3.37 (s, 1H), 2.93 (s, 3H), 2.25 (d, 1H, *J* = 2.8 Hz).

^{13}C NMR ($CDCl_3$, 100 MHz) δ 160.9, 151.3, 139.8 (2C), 130.2 (2C), 129.4 (2C), 123.7, 123.3 (2C), 112.6 (2C), 111.0 (2C), 106.5, 102.9, 100.2, 69.1, 58.0, 55.2, 47.4, 39.9.

ESI *m/z* 517.0 $([M+H])^{+}$, $C_{23}H_{23}Br_2N_2O_2$ requires 517.0).

1-(9H-Carbazol-9-yl)-3-(3,6-dibromo-9H-carbazol-9-yl)propan-2-ol (36)



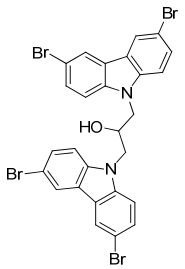
Carbazole (0.026 g, 0.154 mmol) was dissolved in DMF (1.5 mL) and cooled to 0 °C. NaH (60% dispersion in mineral oil, 0.007 g, 0.169 mmol) was added and the reaction was stirred for 1 h at 0 °C. Epoxide **A** (0.059 g, 0.154 mmol) was added and the reaction was stirred at ambient temperature for 21 h. Upon consumption of the starting material by TLC, the reaction was partitioned between EtOAc and H_2O. The aqueous layer was washed 3×EtOAc, and the combined organics were washed with saturated aqueous NaCl, dried over Na_2SO_4, filtered, and concentrated in vacuo. The crude residue was purified by chromatography (SiO_2, 0–20% EtOAc/Hexane) to afford **36** (41 mg, 48%).

^{1}H NMR (acetone-d_6, 400 MHz) δ 8.36 (m, 2H), 8.14 (d, 2H, *J* = 8.0 Hz), 7.63 (d, 2H, *J* = 8.4 Hz), 7.55 (s, 2H), 7.42 (dt, 2H, *J* = 1.2, 7.2 Hz), 7.20 (dt, 2H, *J* = 0.8, 7.2 Hz), 4.76 (m, 1H), 4.64–4.72 (m, 4H), 2.77 (br s, 1H).

^{13}C NMR (acetone-d_6, 100 MHz) δ 142.0 (2C), 141.0 (2C), 129.8 (2C), 126.6 (2C), 124.5 (2C), 124.1 (2C), 123.8 (2C), 121.0 (2C), 119.9 (2C), 112.7 (2C), 112.6 (2C), 110.5 (2C), 70.3, 48.4, 48.1.

ESI *m/z* 591.0 $([M+CO_2H]^{-}$, $C_{28}H_{21}Br_2N_2O_3$ requires 591.0).

1,3-Bis(3,6-dibromo-9H-carbazol-9-yl)propan-2-ol (37)



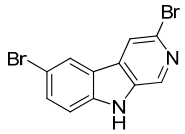
Following a procedure analogous to that used to prepare **36**, **37** was prepared in 34% yield.

^{1}H NMR (acetone-d_6, 400 MHz) δ 8.36 (d, 4H, *J* = 2.0 Hz), 7.64 (d, 4H, *J* = 8.8 Hz), 7.56 (dd, 4H, *J* = 2.0, 8.8 Hz), 4.72 (m, 5H), 2.78 (br s, 1H).

^{13}C NMR (acetone-d_6, 100 MHz) δ 141.2 (4C), 129.8 (4C), 124.6 (4C), 124.1 (4C), 112.9 (4C), 112.7 (4C), 70.3, 48.3 (2C).

ESI *m/z* 747.0 ($[M+CO_2H]^-$, $C_{28}H_{19}Br_4N_2O_3$ requires 746.8).

3,6-Dibromo-β-carboline (Carboline B)

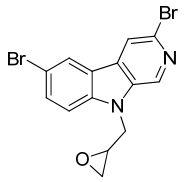


Following a literature procedure[15], β-carboline (0.100 g, 0.595 mmol) and SiO_2 (1.00 g) were suspended in CH_2Cl_2 (15 mL). *N*-Bromosuccinimde (0.212 g, 1.189 mmol) was dissolved in CH_2Cl_2 (15 mL) and the solution was added to the carboline mixture slowly via syringe in the absence of light. The reaction was stirred at ambient temperature for 2.5 h, after which the silica gel was filtered off and washed 3×CH_2Cl_2. The combined organic layer was extracted with 0.1 M NaOH and saturated aqueous NaCl, dried over Na_2SO_4, filtered, and concentrated in vacuo. The crude product was purified by chromatography (SiO_2, 0–100% EtOAc/Hexane) to afford the desired 3,6-dibrominated carboline (25 mg, 13%) as well as 6,8-dibrominated carboline (15 mg, 8%) and the tribrominated carboline (36 mg, 19%).

^{1}H NMR (d_6-DMSO, 500 MHz) δ 8.72 (s, 1H), 8.58 (d, 1H, *J* = 1.5 Hz), 8.48 (s, 1H), 7.70 (dd, 1H, *J* = 1.5, 9.0 Hz), 7.58 (d, 1H, *J* = 9.0 Hz).

ESI *m/z* 326.9 ($[M+H]^+$, $C_{11}H_7Br_2N_2$ requires 326.9).

3,6-Dibromo-9-(oxiran-2-ylmethyl)-9H-pyrido[3,4-b]indole (Epoxide J)

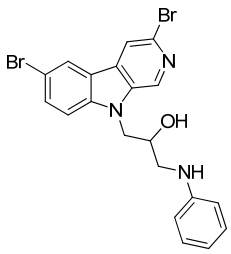


Following Representative Procedure 1, epoxide **J** was prepared from carboline **B** in 73% yield.

^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.62 (d, 1H, *J* = 0.8 Hz), 8.17 (d, 1H, *J* = 2.0 Hz), 8.02 (d, 1H, *J* = 1.2 Hz), 7.69 (dd, 1H, *J* = 2.0, 8.8 Hz), 7.41 (d, 1H, *J* = 8.8 Hz), 5.34 (br s, 1H), 4.73 (dd, 1H, *J* = 2.4, 16.0 Hz), 4.27 (dd, 1H, *J* = 5.2, 16.0 Hz), 3.32 (m, 1H), 2.83 (dd, 1H, *J* = 4.0, 4.4 Hz), 2.49 (dd, 1H, *J* = 2.4, 4.4 Hz).

ESI *m/z* 382.9 ($[M+H]^+$, $C_{14}H_{11}Br_2N_2O$ requires 382.9).

1-(3,6-Dibromo-9H-pyrido[3,4-b]indol-9-yl)-3-(phenylamino)propan-2-ol (38)



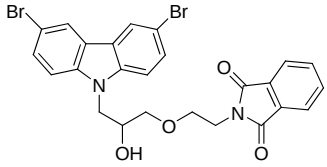
Following Representative Procedure 2, **38** was prepared from epoxide **J** in 14% yield after purification by preparative TLC.

^{1}H NMR ($CDCl_3$, 500 MHz) δ 8.64 (s, 1H), 8.18 (d, 1H, *J* = 2.0 Hz), 7.99 (s, 1H), 7.66 (dd, 1H, *J* = 1.5, 9.0 Hz), 7.40 (d, 1H, *J* = 9.0 Hz), 7.18 (dd, 2H, *J* = 7.5 Hz), 6.76 (t, 1H, *J* = 7.5 Hz), 6.63 (d, 2H, *J* = 8.5 Hz), 5.33 (br s, 1H), 4.38–4.49 (m, 3H), 3.37 (dd, 1H, *J* = 4.0, 13.0 Hz), 3.21 (dd, 1H, *J* = 7.0, 13.0 Hz).

^{13}C NMR ($CDCl_3$, 125 MHz) δ 147.7, 141.2, 137.0, 132.6, 132.5, 130.9, 130.1, 129.7 (2C), 125.0, 122.0, 119.0, 118.6, 113.8 (2C), 113.4, 111.9, 69.6, 48.1, 47.9.

ESI *m/z* 475.9 ($[M+H]^+$, $C_{20}H_{18}Br_2N_3O$ requires 476.0).

2-(2-(3-(3,6-Dibromo-9H-carbazol-9-yl)-2-hydroxypropoxy)ethyl)isoindoline-1,3-dione (39)

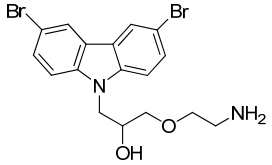


Sodium hydride dispersion (31.6 mg, 0.79 mmol) was added to a solution of *N*-(2-hydroxyethyl)-phthalimide (153.7 mg, 0.80 mmol) in anhydrous THF (1.2 mL, 0.67 M). The suspension is stirred for 15 min before the addition of epoxide **A**. The reaction was stirred at room temperature for 5 min and then at 60 °C for 1 h. The cooled reaction was diluted with EtOAc and washed with water. The aqueous layer was extracted and the combined organics were filtered over a celite pad to afford **39** (44%) which was used without further purification.

^{1}H NMR ($CDCl_3$, 500 MHz) δ 8.12 (s, 2H), 7.85 (s, 2H), 7.72 (m, 2H), 7.55 (d, 2H, *J* = 8.5 Hz), 7.33 (d, 2H, *J* = 8.7 Hz), 4.64 (d, 1H, *J* = 16.1 Hz), 4.27 (d, 1H), 3.88 (m, 4H), 3.31 (br s, 1H), 2.80 (m, 1H), 2.48 (m, 1H), 2.04 (s, 1H).

ESI *m/z* 614.9 ($[M+HCOO]^-$, $C_{26}H_{21}Br_2N_2O_6$ requires 615.0).

1-(2-Aminoethoxy)-3-(3,6-dibromo-9H-carbazol-9-yl)propan-2-ol (40)

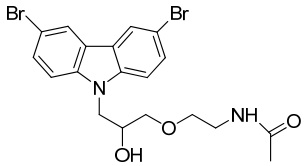


Hydrazine hydrate (400 µL, 8.22 mmol) was added to a solution **39** (53 mg, 0.093 mmol) in ethanol (2.0 mL, 0.046 M). The reaction was stirred overnight, condensed and purified (SiO_2, 5–10% $MeOH/CH_2Cl_2$) to afford **40**.

^{1}H NMR ($CDCl_3$, 500 MHz) δ 8.11 (s, 2H), 7.53 (dd, 2H, *J* = 1.8, 8.7 Hz), 7.38 (d, 2H, *J* = 8.5 Hz), 4.37 (dm, 5H), 4.05 (t, 1H, *J* = 6.8 Hz), 2.84 (m, 2H), 2.62 (m, 1H).

ESI *m/z* 440.9 ($[M+H]^+$, $C_{17}H_{19}Br_2N_2O_2$ requires 441.0).

***N*-(2-(3-(3,6-Dibromo-9H-carbazol-9-yl)-2-hydroxypropoxy)ethyl)acetamide (41)**

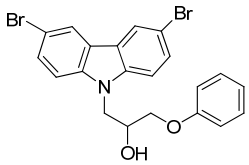


Triethylamine (33.5 µL, 0.26 mmol) and acetic anhydride (17 µL, 0.18 mmol) were added to a solution of **40** (71 mg, 0.16 mmol) in THF (3.0 mL, 0.053 M). The reaction was stirred overnight. The reaction mixture was diluted with EtOAc, washed with water, dried over Na_2SO_4, filtered and condensed. The crude mixture was subjected to flash chromatography (SiO_2, 5% MeOH/CH_2Cl_2).

^{1}H NMR ($CDCl_3$, 500 MHz) δ 8.13 (d, 2H, *J* = 1.7 Hz), 7.55 (dd, 2H, *J* = 1.8, 8.7 Hz), 7.34 (d, 2H, *J* = 9.1 Hz), 5.78 (br s, 1H), 4.35 (ddd, 3H, *J* = 6.2, 6.8 Hz), 4.22 (m, 1H), 3.46 (m, 4H), 3.33 (dd, 1H, *J* = 5.4, 9.7 Hz), 2.80 (br s, 1H), 1.98 (s, 3H).

ESI *m/z* 482.9 ($[M+1]^+$, $C_{19}H_{21}Br_2N_2O_3$ requires 483.0).

1-(3,6-Dibromo-9H-carbazol-9-yl)-3-phenoxypropan-2-ol (42)



Following Representative Procedure 1, **42** was prepared from dibromocarbazole and phenoxymethyloxirane in 61% yield.

^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.14 (d, 2H, *J* = 1.9 Hz), 7.51 (dd, 2H, *J* = 1.9, 8.7 Hz), 7.36 (d, 2H, *J* = 8.8 Hz), 7.127–7.32 (m, 2H), 7.00 (t, 1H, *J* = 7.3 Hz), 6.87 (dd, 2H, *J* = 0.8, 8.9 Hz), 4.58 (dd, 1H, *J* = 7.9, 16.7 Hz), 4.41–4.49 (m, 2H), 4.00 (dd, 1H, *J* = 4.4, 9.6 Hz), 3.89 (dd, 1H, *J* = 4.5, 9.5 Hz), 2.38 (d, 1H, *J* = 5.7 Hz).

^{13}C NMR ($CDCl_3$, 100 MHz) δ 158.0, 139.8, 129.8, 129.4, 123.7, 123.4, 121.8, 114.6, 112.7, 110.8, 69.2, 45.9.

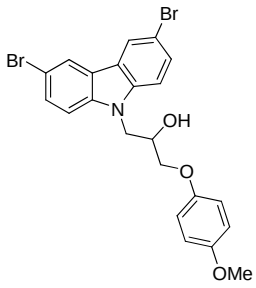
ESI *m/z* 517.9 ($[M+HCOO]^-$, $C_{22}H_{18}Br_2NO_4$ requires 518.0).

(*S*)-**42**: [α] = +16.8 (*c* 3.0, acetone).

(*R*)-**42**: [α] = –14.9 (*c* 3.0, acetone).

Optically active versions of **42** were synthesized from commercially available optically active phenoxymethyl oxirane using the same procedure as described for **42**.

1-(3,6-Dibromo-9H-carbazol-9-yl)-3-(4-methoxyphenoxy)propan-2-ol (43)



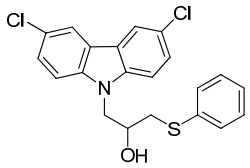
Following Representative Procedure 1, **43** was prepared in 47% yield from dibromocarbazole and (*p*-methoxyphenyl)-glycidyl ether with NaH as the base.

^{1}H NMR ($CDCl_3$, 500 MHz) δ 8.12 (d, 2H, *J* = 2.0 Hz), 7.50 (dd, 2H, *J* = 2.0, 8.5 Hz), 7.34 (d, 2H, *J* = 8.5 Hz), 6.81 (m, 2H), 6.79 (m, 2H), 4.56 (m, 1H), 4.42 (m, 3H), 3.93 (dd, 1H, *J* = 4.5, 9.5 Hz), 3.81 (dd, 1H, *J* = 4.5, 9.5 Hz), 3.76 (s, 3H), 2.39 (d, 1H, *J* = 6.0 Hz).

^{13}C NMR (acetone-d_6, 100 MHz) δ 155.2, 153.8, 141.2 (2C), 129.8 (2C), 124.5 (2C), 124.0 (2C), 116.4 (2C), 115.5 (2C), 112.9 (2C), 112.5 (2C), 71.1, 69.8, 55.9, 47.4.

ESI *m/z* 547.9 ($[M+CO_2H]^-$, $C_{23}H_{20}Br_2NO_5$ requires 548.0).

1-(3,6-Dichloro-9H-carbazol-9-yl)-3-(phenylthio)propan-2-ol (**44**)



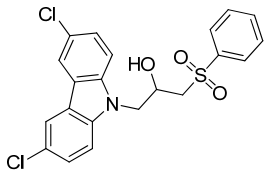
Prepared analogously to **24** affording **44** as a white solid (0.0293 g, 99.0%).

^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.93 (d, 2H, *J* = 1.8 Hz), 7.46–7.14 (m, 9H), 4.41 (dd, 1H, *J* = 4.1, 15.0 Hz), 4.28 (dd, 1H, *J* = 7.0, 15.0 Hz), 4.20–4.06 (m, 1H), 3.09 (dd, 1H, *J* = 5.2, 13.9 Hz), 2.97 (dd, 1H, *J* = 7.2, 13.8 Hz), 2.55 (s, 1H).

^{13}C NMR ($CDCl_3$, 100 MHz) δ 139.7, 134.5, 130.3, 129.5, 127.3, 126.8, 125.4, 123.3, 120.4, 110.6, 69.3, 48.2, 39.4.

ESI *m/z* 446.0 ($[M + HCOO]^-$, $C_{22}H_{18}Cl_2NO_3S$ requires 446.0); 436.0 ($[M + Cl]^-$, $C_{21}H_{17}Cl_3NOS$ requires 436.0).

1-(3,6-Dichloro-9H-carbazol-9-yl)-3-(phenylsulfonyl)propan-2-ol (45)



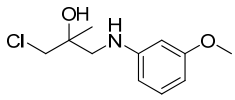
Following the procedure given for **26**, **45** was prepared from **44** in 91% yield.

^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.96 (d, 2H, *J* = 2.0 Hz), 7.80 (d, 2H, *J* = 7.3 Hz), 7.66 (t, 1H, *J* = 7.5 Hz), 7.52 (t, 1H, *J* = 7.9 Hz), 7.40 (dd, 2H, *J* = 2.0, 8.7 Hz), 7.31 (d, 2H, *J* = 8.7 Hz), 4.67 (m, 1H), 4.39 (d, 2H, *J* = 6.3 Hz), 3.29 (d, 1H, *J* = 2.9 Hz), 3.28 (dd, 1H, *J* = 8.3, 14.3 Hz), 3.17 (dd, 1H, *J* = 3.0, 14.2 Hz).

^{13}C NMR ($CDCl_3$, 100 MHz) δ 139.6, 138.8, 134.5, 129.8, 128.0, 127.0, 125.7, 123.5, 120.5, 110.5, 65.8, 60.0, 48.5.

ESI *m/z* 477.9 ($[M + HCOO]^-$; $C_{22}H_{18}Cl_2NO_5S$ requires 478.0).

1-Chloro-3-(3-methoxyphenylamino)-2-methylpropan-2-ol (Chlorohydrin B)

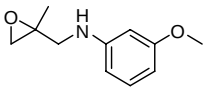


m-Anisidine (0.18 mL, 1.62 mmol) was added to 2-chloromethyl-2-methyl oxirane (0.154 mL, 1.62 mmol) in acetic acid (2 mL) and the mixture was heated to 75 °C. Upon completion the reaction was neutralized with saturated sodium bicarbonate to pH 7, then extracted 3×EtOAc, washed with brine and dried with $MgSO_4$ filtered, and concentrated in vacuo. The crude residue was purified by chromatography (SiO_2, 0–25% EtOAc/Hexane) to afford chlorohydrin **B** (332 mg, 89%).

^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.08 (t, 1H, *J* = 8.1 Hz), 6.29 (m, 2H), 6.23 (t, 1H, *J* = 2.3 Hz), 3.95 (s, NH), 3.77 (s, 3H), 3.64 (d, 1H, *J* = 11.0Hz), 3.56 (d, 1H, *J* = 11.0 Hz), 3.30 (d, 1H, *J* = 13.1 Hz), 3.19 (d, 1H, *J* = 13.2 Hz), 2.31 (apparent d, OH), 1.36 (s, 3H).

ESI *m/z* 230.1 ($[M+H]^+$, $C_{11}H_{17}ClNO_2$ requires 230.1).

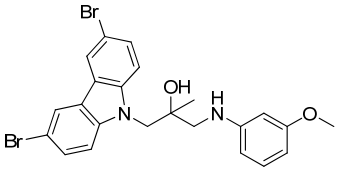
3-Methoxy-*N*-((2-methyloxiran-2-yl)methyl)aniline (Epoxide K)



Chlorohydrin **B** (0.166g, 0.722 mmol) was dissolved in dioxane (1 mL) and added to a solution of KOH (0.168 mg, 3.0 mmol). The reaction was followed by TLC (20% EtOAc/Hexane) until the starting material was consumed and the less polar product was obtained. After aqueous workup, the crude epoxide **K** was used without purification.

^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.07 (t, 1H, *J* = 8.1 Hz), 6.27 (dd, 1H, *J* = 0.8, 8.2 Hz), 6.22 (dd, 1H, *J* = 0.8, 8.2 Hz), 6.16 (t, 1H, *J* = 2.3 Hz), 3.83 (s, 1H), 3.32 (br s, 2H), 2.82 (d, 1H, *J* = 4.5 Hz), 2.63 (d, 1H, *J* = 4.5 Hz).

1-(3,6-Dibromo-9H-carbazol-9-yl)-3-(3-methoxyphenylamino)-2-methylpropan-2-ol (46)



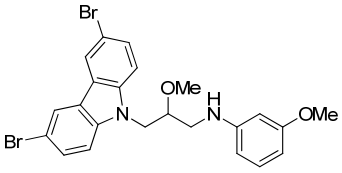
Following Representative Procedure 1, **46** was prepared from epoxide **K i**n 83% yield using NaH as base.

^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.14 (s, 2H), 7.53 (d, 2H, *J* = 8.9 Hz), 7.42 (d, 2H, *J* = 8.4 Hz), 7.09 (t, 1H, *J* = 8.4 Hz), 6.33 (d, 1H, *J* = 6.3 Hz), 6.27 (d, 1H, *J* = 6.3 Hz), 6.18 (s, 1H), 4.41 (d, 1H, *J* = 15.3 Hz), 4.32 (d, 1H, *J* = 15.3 Hz), 3.74 (s, NH), 3.49 (s, 3H), 3.28 (d, 1H, 12.4 Hz), 3.22 (d, 1H, 12.4 Hz), 2.03 (s, OH), 1.33 (s, 3H).

^{13}C NMR ($CDCl_3$, 100 MHz) δ 161.0, 149.8, 140.6 (2C), 130.4 (2C), 129.4 (2C), 123.8 (2C), 123.2 (2C), 112.8, 111.8 (2C), 106.9, 103.8, 99.8, 75.0, 55.4, 52.5, 51.5, 25.1.

ESI *m/z* 516.9 ($[M+H]^+$, $C_{23}H_{23}Br_2N_2O_2$ requires 517.0).

***N*-(3-(3,6-Dibromo-9H-carbazol-9-yl)-2-methoxypropyl)-3-methoxyaniline (47)**



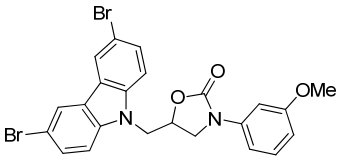
Sodium hydride (9.0 mg, 0.23 mmol) was added to a stirring solution of **7** (99.3 mg, 0.20 mmol) in DMF (0.5 mL, 0.39 M). The solution was stirred at room temperature for 70 min before the dropwise addition of a solution of methyl iodide (14 mL, 0.22 mol) in DMF (1.0 mL). The reaction was monitored by LC/MS for the consumption of SM and the appearance of *O*- and *N*-methyl products. After 2.5 h of stirring at ambient temperature, conversion was about 30% and about 5% *N*-methyl product had formed. The reaction was stopped when an increase of *N*-Me to *O*-Me had been observed and conversion was about 50%. The brown solution was diluted with EtOAc and washed several times with water and brine. The organic layer was dried over Na_2SO_4, filtered and condensed. The mixture was purified by preparative TLC (30% EtOAc/hexanes) to afford **7**.

^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.13 (s, 2H), 7.51 (dd, 2H, *J* = 1.8, 8.8 Hz), 7.31 (d, 2H, *J* = 8.7 Hz), 7.09 (t, 1H, *J* = 8.2 Hz), 6.33 (dd, 1H, *J* = 2.3, 8.3 Hz), 6.21 (dd, 1H, *J* = 2.1, 8.0 Hz), 6.12 (m, 1H), 4.42 (m, 1H), 4.03 (br s, 1H), 3.85 (m, 1H), 3.74 (s, 3H), 3.29 (s, 3H), 3.09 (m, 2H).

^{13}C NMR ($CDCl_3$, 126 MHz) δ 161.0, 149.4, 139.8, 130.4, 129.5, 123.8, 123.5, 112.7, 110.9, 106.7, 103.6, 99.7, 78.2, 58.3, 55.3, 45.3, 44.3.

ESI *m/z* 516.9 ($[M+1]^+$ for $C_{23}H_{22}Br_2N_2O_2$ requires 517.0).

5-((3,6-Dibromo-9H-carbazol-9-yl)methyl)-3-(3-methoxyphenyl)oxazolidin-2-one (48)



Methyl chloroformate (10 μL, 0.13 mmol) was added to a stirring solution of **7** (55.0 mg, 0.11 mmol) and indium powder (3.5 mg, 0.030 mmol) in acetonitrile (3.0 mL), and the reaction mixture was stirred overnight at ambient temperature. An additional 3.1 mg (0.027 mmol) of indium and 20 μL (2.6 eq.) of methyl chloroformate were added. After several hours, the reaction was diluted with EtOAc, washed with water, and then brine. The organic layer was dried over Na_2SO_4, filtered and concentrated. The methyl carbonate was purified via chromatography (SiO_2, 20–40% EtOAc/Hexanes).

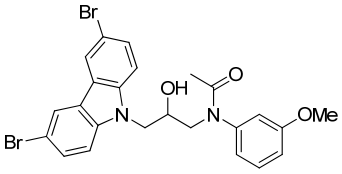
Sodium methoxide (3.0 mL) was added to a solution of carbonate (21.3 mg, 0.038 mmol) and methanol (1.0 mL). After an hour at ambient temperature the solution was diluted with water and extracted with EtOAc. The organic layer was washed with water and brine and condensed to afford **48**.

^{1}H NMR (acetone-d_6, 500 MHz) δ 8.40 (s, 2H), 7.78 (d, 2H, *J* = 8.5 Hz), 7.64 (d, 2H, *J* = 8.9 Hz), 7.23–7.28 (m, 2H), 7.05 (d, 1H, *J* = 8.3 Hz), 6.70 (d, 1H, *J* = 8.3 Hz), 5.24–5.31 (m, 1H), 5.00 (dd, 1H, *J* = 7.9, 15.7 Hz), 4.91 (dd, 1H, *J* = 3.2, 15.8 Hz), 4.38 (t, 1H, *J* = 9.3 Hz), 4.05 (m, 1H), 3.78 (s, 3H).

^{13}C NMR (acetone-d_6, 126 MHz) δ 160.4, 153.9, 140.3, 140.2, 129.8, 129.4, 124.0, 123.5, 112.4, 112.1, 110.3, 109.0, 104.4, 71.9, 54.9, 47.9, 46.6.

ESI *m/z* 528.9 ($[M+1]^+$ for $C_{23}H_{19}Br_2N_2O_3$ calculated 529.0).

***N*-(3-(3,6-Dibromo-9H-carbazol-9-yl)-2-hydroxypropyl)-*N*-(3-methoxyphenyl)acetamide (49)**



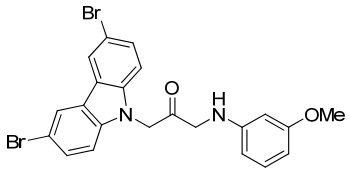
Following a literature procedure[16], Et_3N (14 μL, 0.10 mmol) and acetyl chloride (8 μL, 0.11 mmol) were added to a heterogeneous mixture of substrate **7** (53 mg, 0.11 mmol) and dibutyltin oxide (5.5 mg, 0.022 mmol) in anhydrous toluene (1.5 mL). The reaction vessel was purged with nitrogen, sealed and heated under microwave radiation to 150 °C for 9 min. The reaction was monitored by LC/MS until all starting material had been consumed. The heterogeneous solution was filtered under vacuum to yield a white solid. The crude product was used without purification.

^{1}H NMR ($CDCl_3$, 500 MHz) δ 8.09 (d, 2H, *J* = 1.6 Hz), 7.52 (dd, 2H, *J* = 1.8, 8.7 Hz), 7.29 (d, 2H, *J* = 8.8 Hz), 7.26 (t, 1H, *J* = 8.2 Hz), 6.86 (dd, 1H, *J* = 2.5, 8.4 Hz), 6.68 (dd, 1H, *J* = 1.3, 7.7 Hz), 6.62 (s, 1H,), 4.33–4.40 (m, 1H), 4.29 (dd, 2H, *J* = 2.6, 6.0 Hz), 3.94 (d, 1H, *J* = 4.1 Hz), 3.76 (s, 3H), 3.51 (dd, 1H, *J* = 2.3, 14.0 Hz), 1.9 (s, 3H).

^{13}C NMR ($CDCl_3$, 126 MHz) δ 173.6, 160.9, 144.5, 139.9, 131.0, 129.4, 123.8, 123.4, 119.7, 113.9, 113.5, 112.6, 111.1, 70.9, 55.7, 55.2, 46.0, 22.8.

ESI *m/z* 544.9 ($[M+1]^+$ for $C_{24}H_{22}Br_2N_2O_3$ requires 545.0).

1-(3,6-Dibromo-9H-carbazol-9-yl)-3-(3-methoxyphenylamino)propan-2-one (50)

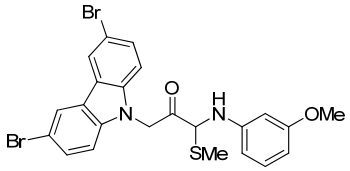


Et_3N (1.65 mL, 11.8 mmol) was added to a stirring solution of **7** (1.02 g, 2.02 mmol) in DMSO (21 mL). The solution was stirred for 30 min before addition of sulfur trioxide pyridine complex (0.659 g, 4.14 mmol). After stirring overnight, additional Et_3N (1.0 mL, 7.17 mmol) was added, followed by sulfur trioxide pyridine complex (0.663 mg, 4.17 mmol) 1 h later. After stirring for 1 h, the orange solution was diluted with ~ 150 mL EtOAc and washed several times with water and then brine. The organic layer was dried over Na_2SO_4, filtered and concentrated to yield brown foam. Flash chromatography (SiO_2, 100% CH_2Cl_2 + 0.2% Et_3N) provided a higher R_f product (methyl thioether **51**, 18%) and a lower R_f ketone (**50**, 40%).

Major product (**50**): ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.18 (d, 2H, *J* = 1.9 Hz), 7.56 (dd, 2H, *J* = 1.9, 8.7 Hz), 7.11 (d, 2H, *J* = 8.8 Hz), 7.06 (t, 1H, *J* = 8.1 Hz), 6.30 (dd, 1H, *J* = 2.3, 8.2 Hz), 6.07 (dd, 1H, *J* = 2.0, 8.0 Hz), 6.11 (t, 1H, *J* = 2.2 Hz), 5.08 (s, 2H,), 4.41 (t, 1H, *J* = 4.8 Hz), 3.90 (d, 2H, *J* = 5.1 Hz), 3.72 (s, 3H).

^{13}C NMR ($CDCl_3$, 126 MHz) δ 202.9, 161.1, 147.9 (2C), 139.5, 130.6 (2C), 129.9 (2C), 124.1(2C), 123.9(2C), 113.5, 110.1(2C), 103.7, 99.3, 55.4, 51.9, 51.0.

ESI *m/z* 500.9 ($[M+1]^+$ for $C_{22}H_{18}Br_2N_2O_2$ requires 501.0).



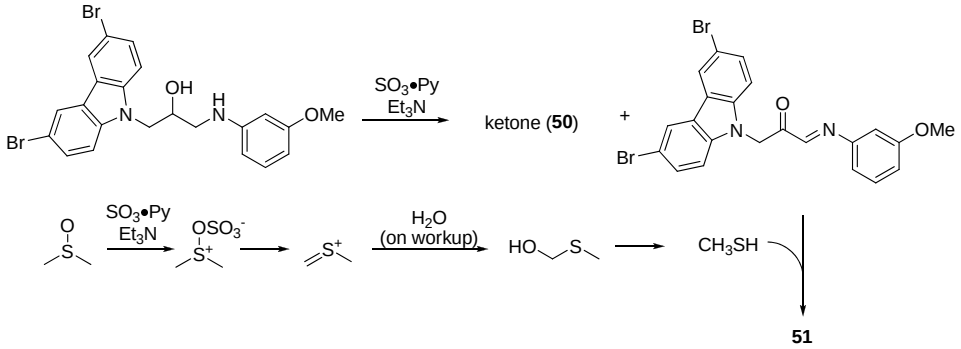
Minor product (**51**): ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.16 (d, 2H, *J* = 2.0 Hz), 7.55 (dd, 2H, *J* = 1.7, 8.8 Hz), 7.25 (d, 2H, *J* = 8.8 Hz), 7.12 (t, 1H, *J* = 8.4 Hz), 6.39 (dd, 1H, *J* = 2.2, 8.2 Hz), 6.33 (dd, 1H, *J* = 2.2, 8.0 Hz), 6.29 (t, 1H, *J* = 2.2 Hz), 5.50 (d, 1H, *J* = 18.0 Hz), 5.22 (d, 1H, *J* = 18.4 Hz), 5.25 (d, 1H, *J* = 8.0 Hz), 4.50 (d, 1H, *J* = 8.0 Hz, exchangeable), 3.76 (s, 3H), 1.74 (s, 3H).

^{13}C NMR ($CDCl_3$, 126 MHz) δ 193.2, 160.9, 143.9 (2 C), 139.8(2C), 130.4, 129.8(2C), 124.1, 123.7(2C), 113.4(2C), 110.3(2C), 107.8, 104.7, 101.0, 60.3, 55.4, 48.9, 9.0.

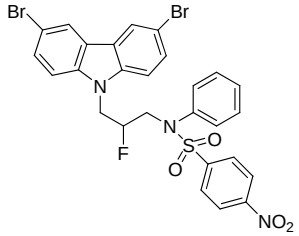
ESI *m/z* 498.9 $[M-SMe+H]^+$ ([M-SMe+H]+ for $C_{23}H_{20}Br_2N_2O_2S$ requires 499.0.

HRMS *m/z*: 546.9675 $[M+H]^+$ ([M+H]$^+$ for $C_{23}H_{20}Br_2N_2O_2S$ requires 545.9612).

Proposed mechanism for generation of 51:



***N*-(3-(3,6-Dibromo-9H-carbazol-9-yl)-2-fluoropropyl)-4-nitro-*N*-phenylbenzenesulfonamide (Ns-C)**

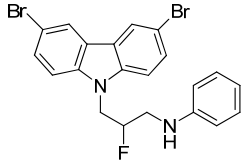


Prepared from epoxide **A** and Ns-aniline via Representative Procedures 3 and 4. Crude mixture was purified by chromatography (SiO_2, 40% EtOAc/Hexanes + 0.1% Et_3N) to afford Ns-**C** in 60% yield.

^{1}H NMR (acetone-d_6, 400 MHz) δ 8.37 (m, 2H), 7.90 (m, 2H), 7.68 (m, 1H), 7.53–7.60 (m, 6H), 7.32–7.40 (m, 5H), 5.03 (dm, 1H, J = 48.1 Hz), 4.71–4.93 (m, 2H), 4.27–4.41 (m, 2H).

ESI *m/z* 703.9 ($[M+HCOO]^-$; $C_{28}H_{21}Br_2FN_3O_6S$ requires 704.0).

***N*-(3-(3,6-Dibromo-9H-carbazol-9-yl)-2-fluoropropyl)aniline (52)**



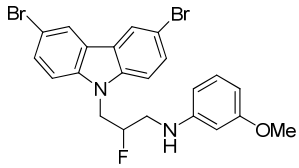
Cesium carbonate (11.5 mg, 0.036 mmol), Ns-**C** (7.9 mg, 0.012 mmol), THF (0.7 mL, 0.017 M) and benzenethiol (3.8 µL, 0.037 mmol) were combined and stirred overnight. The crude reaction mixture was diluted with EtOAc, washed with water and brine. The organic layer was dried over Na_2SO_4, filtered and condensed. Chromatographic purification (SiO_2, 20% EtOAc/Hexanes + 0.2% Et_3N) provided **52** (4.2 mg, 74%).

^{1}H NMR ($CDCl_3$, 500 MHz) δ 8.16 (s, 2H), 7.56 (d, 2H, J = 8.5 Hz), 7.31 (d, 2H, J = 8.5 Hz), 7.21 (t, 2H, J = 7.4 Hz), 6.80 (t, 1H, J = 7.3 Hz), 6.62 (d, 2H, J = 8.5 Hz), 5.11 (dddd, 1H, J = 5.4, 5.4, 10.4, 47.4 Hz), 4.52–4.68 (m, 2H), 3.94 (t, 1H, J = 6.0 Hz), 3.30–3.51, (dm, 2H).

^{13}C NMR ($CDCl_3$, 100 MHz) δ 147.2, 139.6, 129.6, 129.5, 123.8, 123.5, 118.9, 113.5, 112.9, 110.6 (d, ^4J = 2.0 Hz), 90.8 (d, ^1J = 176.9 Hz), 45.6 (d, ^2J = 23.1 Hz), 45.1 (d, ^2J = 25.1 Hz).

ESI *m/z* 475.0 ($[M+H)^+$; $C_{21}H_{18}Br_2FN_2$ requires 475.0).

***N*-(3-(3,6-Dibromo-9H-carbazol-9-yl)-2-fluoropropyl)-3-methoxyaniline (53)**



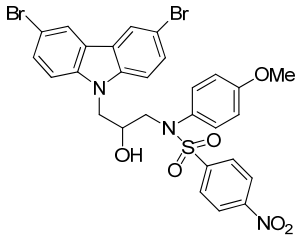
Following Representative Procedure 5, **53** was prepared from Ns-**B** in 88%.

^{1}H NMR ($CDCl_3$, 500 MHz) δ 8.16 (d, 2H, J = 2.0 Hz), 7.56 (dd, 2H, J = 1.9, 8.7 Hz), 7.31 (d, 2H, J = 8.6 Hz), 7.11 (t, 1H, J = 8.1 Hz), 6.36 (dd, 1H, J = 2.2, 8.1 Hz), 6.23 (dd, 1H, J = 2.0, 8.0 Hz), 6.15 (t, 1H, J = 2.3 Hz), 5.11 (dddd, 1H, J = 4.6, 5.8, 10.4, 47.7 Hz), 4.60 (m, 2H), 4.39 (dm, 2H), 3.95 (t, 1H, J = 6.3 Hz), 3.75 (s, 3H).

^{13}C NMR ($CDCl_3$, 100 MHz) δ 161.0, 148.6, 139.6, 130.4, 129.6, 123.9, 123.5, 112.9, 110.6 (d, ^4J = 2.0 Hz), 106.5, 103.9, 99.7, 90.7 (d, ^1J = 176.9 Hz), 55.3, 45.6 (d, ^2J = 22.1 Hz), 45.1 (d, ^2J = 25.1 Hz).

ESI *m/z* 504.9 ($[M+H]^+$, $C_{22}H_{20}Br_2FN_2O$ requires 505.0).

***N*-(3-(3,6-Dibromo-9H-carbazol-9-yl)-2-hydroxypropyl)-*N*-(4-methoxyphenyl)-4-nitrobenzenesulfonamide (Ns-D).**

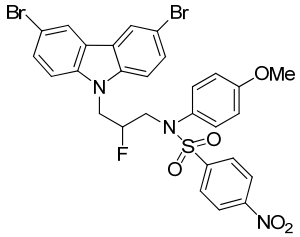


Prepared from epoxide **A** and Ns-anisidine according to Representative Procedure 3 in71% yield.

^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.29 (d, 2H, *J* = 8.7 Hz), 8.11 (d, 2H, *J* = 1.9 Hz), 7.71 (d, 2H, *J* = 8.6 Hz), 7.52 (dd, 2H, *J* = 1.9, 8.6 Hz), 7.23 (d, 2H, *J* = 8.9 Hz), 6.94 (d, 2H, *J* = 8.9 Hz), 6.82 (d, 2H, *J* = 8.9 Hz), 4.44 (dd, 1H, *J* = 3.8, 14.8 Hz), 4.30 (m, 1H), 4.21 (br s, 1H), 3.81 (s, 3H), 3.69 (m, 2H).

ESI *m/z* 732.0 ($[M+HCOO]^-$; $C_{29}H_{24}Br_2N_3O_8S$ requires 732.0).

***N*-(3-(3,6-Dibromo-9H-carbazol-9-yl)-2-fluoropropyl)-*N*-(4-methoxyphenyl)-4-nitrobenzenesulfonamide (Ns-E)**

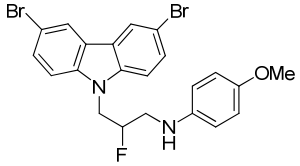


Prepared from Ns-**D** according to Representative Procedure 4 in 62% yield.

^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.27 (m, 2H), 8.09 (m, 2H), 7.71 (d, 2H, *J* = 7.4 Hz), 7.53 (m, 2H), 7.19 (m, 2H), 6.95 (d, 2H, *J* = 8.8 Hz), 6.82 (d, 2H, *J* = 8.8 Hz), 4.92 (dm, 1H, J_d = 48.3 Hz), 4.55 (m, 2H), 3.88 (m, 2H), 3.79 (s, 3H).

ESI *m/z* 734.0 ($[M+HCOO]^-$, $C_{29}H_{23}Br_2FN_3O_7S$ requires 689.0).

***N*-(3-(3,6-Dibromo-9H-carbazol-9-yl)-2-fluoropropyl)-4-methoxyaniline (54)**



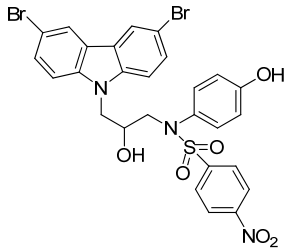
Prepared from Ns-**E** according to Representative Procedure 5 in 70% yield.

^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.14 (m, 2H), 7.53 (dt, 2H, *J* = 1.6, 8.8 Hz), 7.30 (d, 2H, *J* = 8.6 Hz), 6.78 (d, 2H, *J* = 7.9 Hz), 6.57 (d, 2H, *J* = 7.9 Hz), 5.07 (dddd, 1H, *J* = 4.7, 6.1, 9.4, 47.7 Hz), 4.58 (m, 2H), 3.75 (s, 3H), 3.32 (m, 2H).

^{13}C NMR ($CDCl_3$, 100 MHz) δ 153.2, 141.3, 139.7, 129.6, 123.9, 123.5, 115.1, 115.1, 112.9, 110.7 (d, ^4J = 2.0 Hz), 90.9 (d, ^1J = 175.9 Hz), 55.9, 46.8 (d, ^2J = 22.1 Hz), 45.0 (d, ^1J = 25.1 Hz).

ESI *m/z* 549.0 ($[M+HCOO]^-$, $C_{23}H_{20}Br_2FN_2O_3$ requires 549.0).

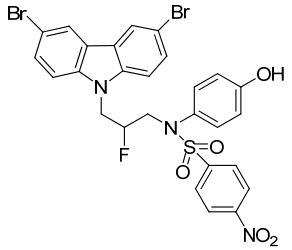
***N*-(3-(3,6-Dibromo-9H-carbazol-9-yl)-2-hydroxypropyl)-*N*-(4-hydroxyphenyl)-4-nitrobenzenesulfonamide (Ns-F)**



Boron tribromide (50 μL, 0.53 mmol) was added dropwise to a cooled solution of Ns-**D** (95.0 mg, 0.14 mmol) in dry CH_2Cl_2 (2.5 mL, 0.055 M) in a 20 mL vial. The reaction was warmed gently in the melting ice bath. All starting material had been consumed after 2.5 h. The reaction mixture was diluted with EtOAc and washed with water, followed by saturated sodium bicarbonate solution and another water wash and brine. The organic was dried over Na_2SO_4, filtered and condensed. The crude material was purified by chromatography (SiO_2, 1% MeOH/CH_2Cl_2) to afford Ns-**F** in 70% yield.

^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.29 (d, 2H, *J* = 8.7 Hz), 8.11 (d, 2H, *J* = 1.9 Hz), 7.71 (d, 2H, *J* = 8.6 Hz), 7.52 (dd, 2H, *J* = 8.6, 1.9 Hz), 7.23 (d, 2H, *J* = 8.9 Hz), 6.94 (d, 2H, *J* = 8.9 Hz), 6.82 (d, 2H, *J* = 8.9 Hz), 4.44 (dd, 1H, *J* = 14.8, 3.8 Hz), 4.30 (m, 1H), 4.21 (br s, 1H), 3.81 (s, 3H), 3.69 (m, 2H).

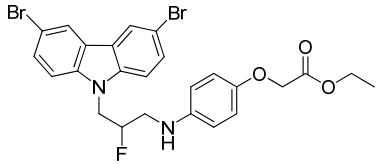
***N*-(3-(3,6-Dibromo-9H-carbazol-9-yl)-2-fluoropropyl)-*N*-(4-hydroxyphenyl)-4-nitrobenzenesulfonamide (Ns-G)**



Ns-**G** was prepared via Representative Procedure 4 (using Morpho-DAST). Crude material was purified by chromatography (SiO_2, 1% MeOH/CH_2Cl_2 +0.2% Et_3N) to afford Ns-**G** in 89% yield.

^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.48 (d, 2H, *J* = 8.8 Hz), 8.41, (d, 2H, *J* = 1.7 Hz), 7.95 (d, 2H, *J* = 8.9 Hz), 7.66 (dd, 2H, *J* = 2.0, 8.7 Hz), 7.10 (d, 2H, *J* = 8.8 Hz), 6.89 (d, 2H, *J* = 8.9 Hz), 5.10 (dddd, 1H, *J* = 3.6, 7.3, 11.0, 49.6 Hz), 4.74–4.89 (m, 2H), 4.16–4.33 (m, 2H), 3.09 (br s, 1H).

Ethyl 2-(4-(3-(3,6-Dibromo-9H-carbazol-9-yl)-2-fluoropropylamino)phenoxy)acetate (55)



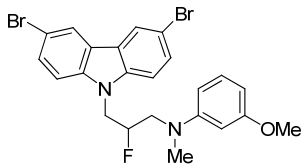
Following Representative Procedure 5, **55** was prepared from **74**.

^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.09 (d, 2H, *J* = 1.8 Hz), 7.50 (dd, 2H, *J* = 5.4 Hz), 7.23 (d, 2H, *J* = 5.4 Hz), 6.77 (d, 2H, *J* = 9.0 Hz), 6.51 (d, 2H, *J* = 8.8 Hz), 5.03 (dp, 1H, *J* = 5.8, 9.7, 47.5 Hz), 4.44–4.62 (m, 5H), 4.23 (q, 2H, *J* = 7.3 Hz), 3.15–3.41 (m, 2H), 1.26 (t, 3H, *J* = 7.0 Hz).

^{13}C NMR ($CDCl_3$, 100 MHz) δ 169.5, 151.3, 142.2, 139.6, 129.5, 123.9, 123.5, 116.4, 114.8, 112.9, 110.6 (d, ^4J = 1.4 Hz), 90.8 (d, ^1J = 176.4 Hz), 66.6, 61.4, 46.4 (d, ^2J = 22.1 Hz), 45.0 (d, ^1J = 25.4 Hz).

ESI *m/z* 620.9 ($[M+HCOO]^-$, $C_{26}H_{24}Br_2FN_2O_5$ requires 621.0).

_N_-(3-(3,6-Dibromo-9H-carbazol-9-yl)-2-fluoropropyl)-3-methoxy-_N_-methylaniline (56)



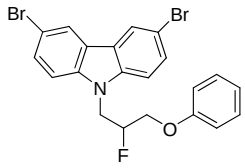
Prepared from **35** following Representative Procedure 4 in 71% yield.

^{1}H NMR ($CDCl_3$, 500 MHz) δ 8.13 (d, 2H, *J* = 1.9 Hz), 7.54 (dd, 2H, *J* = 1.9, 8.8 Hz), 7.23 (d, 2H, *J* = 8.7 Hz), 7.12 (t, 1H, *J* = 8.2 Hz), 6.32 (dd, 1H, *J* = 2.2, 8.1 Hz), 6.26 (dd, 1H, *J* = 2.3, 8.0 Hz), 6.17 (t, 1H, *J* = 2.4 Hz), 5.10 (dddd, 1H, *J* = 4.6, 6.4, 10.7, 48.5 Hz), 4.37–4.48 (m, 2H), 3.72 (s, 3H), 3.60–3.71 (m, 1H), 3.53 (dt, 1H, *J* = 6.9, 15.9 Hz), 2.99 (s, 3H).

^{13}C NMR ($CDCl_3$, 126 MHz) δ 158.5, 147.8, 137.1, 127.8, 127.0, 121.4, 120.9, 110.4, 108.2, 103.3, 99.9, 97.1, 88.7 (d, $^1J_{C\text{-}F}$ = 188 Hz), 52.7, 52.3 (d, $^2J_{C\text{-}F}$ = 25 Hz), 43.5, 43.3 (d, $^2J_{C\text{-}F}$ = 25 Hz).

ESI *m/z* 518.9 ($[M+H]^+$ for $C_{23}H_{22}Br_2FN_2O$ requires 519.0).

3,6-Dibromo-9-(2-fluoro-3-phenoxypropyl)-9H-carbazole (57)



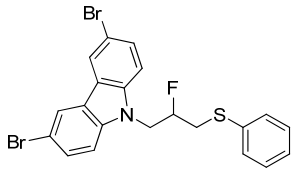
Prepared from **42** following Representative Procedure 4. The crude mixture was purified by chromatography (SiO_2, 100% CH_2Cl_2 + 0.2% Et_3N) to afford **57** in 97% yield.

^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.13 (d, 2H, *J* = 1.7 Hz), 7.51 (dd, 2H, *J* = 1.9, 8.7 Hz), 7.29–7.35 (m, 4H), 7.01 (t, 1H, *J* = 7.5 Hz), 6.91 (d, 1H, *J* = 7.8 Hz), 5.16 (dddd, 1H, *J* = 4.5, 5.4, 9.7, 46.0 Hz), 4.59–4.79 (m, 2H), 4.03–4.17 (m, 2H).

^{13}C NMR ($CDCl_3$, 100 MHz) δ 157.9, 139.8, 129.9, 129.5, 123.9, 123.4, 122.0, 114.7, 112.9, 110.8 (d, ^4J = 2.0 Hz), 89.7 (d, ^1J = 179.0 Hz), 66.2 (d, ^2J = 26.1 Hz), 44.3 (d, ^2J = 24.1 Hz).

ESI *m/z* 519.9 ($[M+HCOO)^-$, $C_{22}H_{17}Br_2FNO_3$ requires 520.0).

3,6-Dibromo-9-(2-fluoro-3-(phenylthio)propyl)-9H-carbazole (Fluoride A)

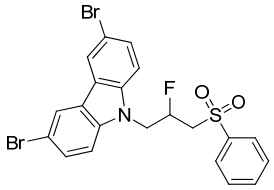


Fluorination of **44** following Representative Procedure 4 afforded fluoride **A** in 28% yield owing to elimination and rearrangement products.

^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.13 (d, 2H, *J* = 1.9 Hz), 7.54 (dd, 2H, *J* = 1.9, 8.7 Hz), 7.42 (dt, 2H, *J* = 2.0, 3.2 Hz), 7.36–7.27 (m, 5H), 5.04–4.81 (m, 1H), 4.66 (ddd, 1H, *J* = 2.8, 15.9, 26.6 Hz), 4.53 (ddd, 1H, *J* = 6.7, 15.9, 20.8 Hz), 3.37–3.23 (m, 1H), 3.09 (ddd, 1H, *J* = 8.4, 11.3, 14.2 Hz).

^{13}C NMR ($CDCl_3$, 100 MHz) δ 139.8, 134.3, 129.6, 129.5, 127.6, 123.9, 123.4, 112.9, 110.9 (d, *J* = 2.1 Hz) 92.2, 90.4, 46.2 (d, *J* = 22.8 Hz) 35.6 (d, *J* = 23.3 Hz).

3,6-Dibromo-9-(2-fluoro-3-(phenylsulfonyl)propyl)-9H-carbazole (58)



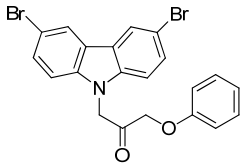
To a solution of fluoride **A** (0.0143 g, 0.0290 mmol) in 0.5 mL CH_2Cl_2, a solution of *m*CPBA (77%, 0.0162 g, 0.0725 mmol) in 0.5 mL CH_2Cl_2 was added dropwise. The mixture was sealed and stirred at rt overnight. The crude was diluted with 30 mL EtOAc and washed with saturated $NaHCO_3$ 3×30 mL and brine 1×30 mL. The organic layer was dried over anhydrous Na_2SO_4 and evaporated to afford the crude product, which was purified by chromatography (SiO_2, EtOAc/Hexanes) to afford white solid as product (0.0114 g, yield 75%).

^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.12 (s, 2H, *J* = 2.0 Hz), 7.90 (d, 2H, *J* = 8.0 Hz), 7.68 (t, 1H, *J* = 7.4 Hz), 7.63–7.53 (m, 4H), 7.34 (d, 2H, *J* = 8.7 Hz), 5.38 (dd, 1H, *J* = 5.9, 47.1 Hz), 4.72 (dd, 1H, *J* = 15.9, 26.8 Hz), 4.56 (ddd, 1H, *J* = 6.6, 16.0, 22.4 Hz), 3.61–3.40 (m, 2H).

^{13}C NMR ($CDCl_3$, 100 MHz) δ 139.8, 139.1 (d, *J* = 1.6 Hz), 134.7, 129.8, 129.8, 128.2, 124.1, 123.5, 113.3, 110.9 (d, *J* = 2.1 Hz), 87.2 (d, *J* = 182.1 Hz), 58.3 (d, *J* = 23.7 Hz), 47.2 (d, *J* = 22.5 Hz).

ESI *m/z* 557.9 ($[M + Cl]^-$, $C_{21}H_{16}Br_2ClFNO_2S$ requires 557.9).

1-(3,6-Dibromo-9H-carbazol-9-yl)-3-phenoxypropan-2-one (59)

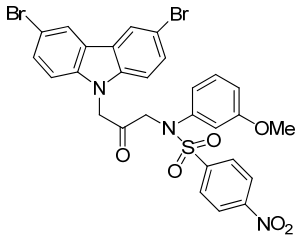


Dess-Martin periodinane (58.2 mg, 0.137 mmol) was charged to a solution of **42** (45.0 mg, 0.095 mmol) in CH_2Cl_2 (1.0 mL, 0.095 M). After 2 h the reaction mixture was diluted with EtOAc and washed with a saturated sodium thiosulfate solution, water and brine. The organic layer was dried over Na_2SO_4, filtered and condensed. The crude product was used without additional purification (74% yield).

^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.15 (d, 2H, *J* = 1.9 Hz), 7.52 (dd, 2H, *J* = 1.9, 8.6 Hz), 7.35 (m, 2H), 7.08 (t, 1H, *J* = 7.3 Hz), 7.04 (d, 2H, *J* = 8.9 Hz), 6.91 (m, 2H), 5.29 (s, 2H), 4.68 (m, 2H).

ESI *m/z* 469.9 ($[M–H]^-$, $C_{21}H_{15}Br_2NO_2$ requires 470.0).

***N*-(3-(3,6-Dibromo-9H-carbazol-9-yl)-2-oxopropyl)-*N*-(3-methoxyphenyl)-4-nitrobenzenesulfonamide (60)**

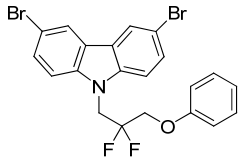


Ns-**A** was oxidized with Dess-Martin periodinane as described for **59** to afford **60** in quantitative yield.

^{1}H NMR ($CDCl_3$, 500 MHz) δ 8.24 (d, 2H, *J* = 8.9 Hz), 8.14 (s, 2H), 7.68 (d, 2H, *J* = 9.1 Hz), 7.53 (d, 2H, *J* = 8.6 Hz), 7.18 (t, 1H, *J* = 8.7 Hz), 7.05 (t, 2H, *J* = 8.1 Hz), 6.87 (dd, 1H, *J* = 8.3, 2.5 Hz), 5.21, (s, 2H), 4.30 (s, 2H), 2.48 (s, 3H).

ESI *m/z* 683.9 ($[M–H]^-$, $C_{28}H_{20}Br_2N_3O_6S$ requires 684.0).

3,6-Dibromo-9-(2,2-difluoro-3-phenoxypropyl)-9H-carbazole (61)



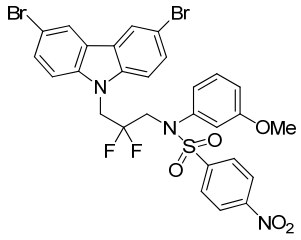
Diethylaminosulfur trifluoride (39 µL, 0.30 mmol) was added dropwise to a solution of **59** (33.3 mg, 0.070 mmol) in anhydrous CH_2Cl_2 (1.5 mL, 0.047 M). The reaction was quenched with saturated sodium bicarbonate solution, and then extracted 3×CH_2Cl_2. The organic layer was dried over Na_2SO_4, filtered and condensed. The crude mixture was purified by chromatography (SiO_2, 10% EtOAc/Hexanes + 0.2% Et_3N) to afford **61** in 69% yield.

^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.09 (d, 2H, *J* = 1.9 Hz), 7.48 (dd, 2H, *J* = 1.8, 8.7 Hz) 7.30–7.40 (m, 4H), 7.06 (t, 1H, *J* = 7.3 Hz), 6.91 (d, 2H, *J* = 7.9 Hz), 4.79 (t, 2H, *J* = 12.4 Hz), 4.07 (t, 2H, *J* = 11.1 Hz).

^{13}C NMR ($CDCl_3$, 100 MHz) δ 157.2, 140.0, 130.0, 129.6, 124.1, 123.3, 122.6, 114.8, 113.4, 111.1 (d, ^4J = 1.0 Hz), 66.10 (t, ^2J = 34.2 Hz), 45.4 (t, ^2J = 31.2 Hz).

ESI *m/z* 537.9 ([M+HCOO]$^-$, $C_{22}H_{16}Br_2F_2NO_3$ requires 538.0).

***N*-(3-(3,6-Dibromo-9H-carbazol-9-yl)-2,2-difluoropropyl)-*N*-(3-methoxyphenyl)-4-nitrobenzenesulfonamide (Ns-H)**

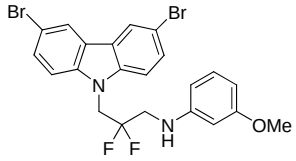


Ns-**H** was prepared from **60** as described for **61** in quantitative yield and the crude product was used without additional purification.

^{1}H NMR ($CDCl_3$, 500 MHz) δ 8.31 (d, 2H, *J* = 8.9 Hz), 8.11 (s, 2H), 7.77 (d, 2H, *J* = 8.9 Hz), 7.55 (dd, 2H, *J* = 1.8, 8.7 Hz), 7.25 (m, 3H), 6.92 (dd, 1H, *J* = 2.0, 8.3 Hz), 6.73 (m, 1H) 6.61, (d, 1H, *J* = 7.7 Hz), 4.78 (t, 2H, *J* = 14.7 Hz), 4.18 (t, 2H, *J* = 11.2 Hz), 3.78 (s, 3H).

ESI *m/z* 751.9 ([M+HCOO]$^-$, $C_{29}H_{22}Br_2F_2N_3O_7S$ requires 752.0).

***N*-(3-(3,6-Dibromo-9H-carbazol-9-yl)-2,2-difluoropropyl)-3-methoxyaniline (62)**



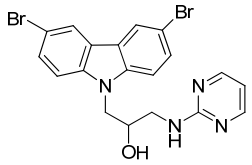
The nosyl group on Ns-**H** was removed according to Representative Procedure 5 to afford **62** in 35% yield.

^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.11 (d, 2H, *J* = 1.6 Hz), 7.49 (dd, 2H, *J* = 2.0, 8.7 Hz), 7.32 (d, 2H, *J* = 8.9 Hz), 7.11 (t, 1H, *J* = 8.2 Hz) 6.39 (dd, 1H, *J* = 2.3, 8.2 Hz), 4.68 (t, 2H, *J* = 13.2 Hz), 3.89 (t, 1H, *J* = 7.0 Hz), 3.74 (s, 3H), 3.47 (m, 2H).

^{13}C NMR ($CDCl_3$, 100 MHz) δ 161.0, 148.0, 140.0, 130.5, 129.7, 129.5, 124.1, 123.3, 113.4, 112.4, 111.2, 104.7, 100.3, 55.3, 46.7 (t, ^2J = 29.2 Hz), 46.0 (t, ^2J = 30.2 Hz).

ESI *m/z* 566.9 ([M+HCOO]$^-$, $C_{23}H_{19}Br_2F_2N_2O_3$ requires 567.0).

1-(3,6-Dibromo-9H-carbazol-9-yl)-3-(pyrimidin-2-ylamino)propan-2-ol (63)



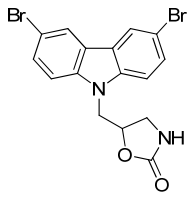
To a 4 mL vial was added **28** (34.8 mg, 0.087 mmol), 2-chloropyrimidine (10.3 mg, 0.090 mmol) and DMF (1.5 mL, 0.058 M). The reaction was heated at 100 °C overnight. The cooled reaction mixture was diluted with EtOAc and washed several times with water and brine. The organic layer was dried over Na_2SO_4, filtered and condensed. The crude mixture was subjected to chromatography (SiO_2, 20% MeOH/CH_2Cl_2).

^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.26 (d, 2H, *J* = 4.9 Hz), 8.14 (d, 2H, *J* = 1.9 Hz), 7.56 (dd, 2H, *J* = 1.9, 6.7 Hz), 7.37 (d, 2H, *J* = 8.7 Hz), 6.63 (t, 1H, *J* = 4.9 Hz), 5.43 (t, 1H, *J* = 5.7 Hz), 4.36 (s, 3H), 3.56 (m, 1H), 3.30–3.38 (m, 1H).

^{13}C NMR ($CDCl_3$, 126 MHz) δ 139.4, 129.5 (2C), 129.3 (2C), 123.7 (2C), 123.4 (2C), 118.6 (2C), 113.5 (2C), 112.3, 110.7 (2C), 67.6, 50.9, 33.6.

ESI *m/z* 474.9 ($[M+H]^+$, $C_{19}H_{17}Br_2N_4O$ requires 475.0).

5-((3,6-Dibromo-9H-carbazol-9-yl)methyl)oxazolidin-2-one (Oxazolidinone A)

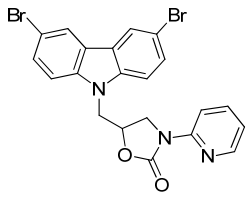


A solution of triphosgene (0.0890 g, 0.300 mmol, 0.35 equiv) in 2 mL anhydrous CH_2Cl_2 was added dropwise to a solution of **28** (0.3413 g, 0.857 mmol) and Et_3N (0.1909 g, 1.886 mmol) in 1 mL CH_2Cl_2 under N_2 atmosphere at 4 °C. The reaction mixture was stirred for 15 min at 4 °C and then warmed to room temperature and stirred for 1 hour. CH_2Cl_2 was removed under vacuum. Saturated NH_4Cl (5 mL) and 10 mL EtOAc were added to the residue and stirred for 20 min. The aqueous layer was separated and the organic layer was washed with water 2×10 mL. The combined aqueous layers were extracted with EtOAc, dried over anhydrous Na_2SO_4 and evaporated to afford the crude product, which was purified by chromatography (SiO_2, CH_2Cl_2/EtOAc) to afford oxazolidinone **A** as a white solid (117 mg, 20% over 2 steps).

^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.14 (d, 2H, *J* = 1.9 Hz), 7.58 (dd, 2H, *J* = 1.9, 8.7 Hz), 7.31 (d, 2H, *J* = 8.7 Hz), 5.05–5.14 (m, 1H), 5.02 (br s, 1H), 4.54 (dd, 2H, *J* = 5.2, 1.8 Hz), 3.67 (t, 1H, *J* = 8.5 Hz), 3.37 (dd, 1H, *J* = 6.3, 9.0 Hz).

ESI *m/z* 466.9 ($[M+HCOO]^-$, $C_{17}H_{13}Br_2N_2O_4$ requires 466.9).

5-((3,6-Dibromo-9H-carbazol-9-yl)methyl)-3-(pyridin-2-yl)oxazolidin-2-one (Oxazolidinone B)

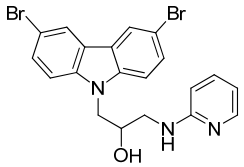


Following a literature procedure[17], a mixture of oxazolidinone **A** (0.0195 g, 0.0460 mmol), 2-iodopyridine (0.0209 g, 0.102 mmol), CuI (0.0009 g, 0.00460 mmol), and K_2CO_3 (0.0058 g, 0.0418 mmol,) in 0.5 mL of DMSO was sealed tightly in a vial and heated at 130 °C for 12 h. The reaction mixture was cooled and diluted with 20 mL EtOAc and washed 5×10 mL water. The organic layer was dried over anhydrous Na_2SO_4 and evaporated to afford the crude product, which was purified by chromatography (SiO_2, CH_2Cl_2/EtOAc) to afford oxazolidinone **B** as a white solid (0.0183 g, 79%).

^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.25 (d, 1H, *J* = 4.9 Hz), 8.13 (d, 2H, *J* = 1.3 Hz), 8.11 (s, 1H), 7.68 (t, 1H, *J* = 7.9 H), 7.59 (dd, 2H, *J* = 1.7, 8.7 Hz), 7.35 (d, 2H, *J* = 8.7 Hz), 7.02 (t, 1H, *J* = 6.1 Hz), 5.02–5.16 (m, 1H), 4.60 (d, 2H, *J* = 5.0 Hz), 4.36 (dd, 1H, *J* = 8.7, 10.7 Hz), 4.04 (dd, 1H, *J* = 7.1, 10.8 Hz).

ESI *m/z* 543.9 ($[M + HCOO]^-$, $C_{22}H_{16}Br_2N_3O_4$ requires 544.0).

1-(3,6-Dibromo-9H-carbazol-9-yl)-3-(pyridin-2-ylamino)propan-2-ol (64)



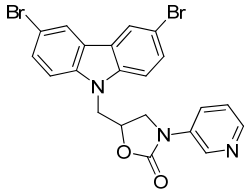
LiOH·H_2O (0.0076 g, 0.182 mmol, 10 equiv) was added to oxazolidinone **B** (0.0091 g, 0.0182 mmol) in a mixture of 208 µL THF and 23 µL H_2O (v/v = 9:1). The mixture was stirred at room temperature for 7 d. The reaction mixture was purified by chromatography (SiO_2, 1:1 CH_2Cl_2/EtOAc + 1% Et_3N) to afford **64** as a white solid (0.0071 g, 41%).

^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.14 (d, 2H, *J* = 1.9 Hz), 8.04 (d, 1H, *J* = 4.5 Hz), 7.56 (dd, 2H, *J* = 1.9, 8.7 Hz), 7.40–7.48 (m, 1H), 7.37 (d, 2H, *J* = 8.7 Hz), 6.66 (t, 1H, *J* = 6.2 Hz), 6.46 (d, 1H, *J* = 8.0 Hz), 4.52 (t, 1H, *J* = 5.0 Hz), 4.26–4.41 (m, 3H), 3.44 (dd, 1H, *J* = 5.0, 15.2 Hz), 3.15–3.32 (m, 1H), 2.27–2.44 (m, 1H).

^{13}C NMR ($CDCl_3$, 100 MHz) δ 158.6, 146.7, 139.5, 138.1, 129.2, 123.6, 123.3, 113.9, 112.3, 110.9, 109.6, 70.5, 47.4, 46.8.

ESI *m/z* 518.0 ($[M + HCOO]^-$, $C_{21}H_{18}Br_2N_3O_3$ requires 518.0).

5-((3,6-Dibromo-9H-carbazol-9-yl)methyl)-3-(pyridin-3-yl)oxazolidin-2-one (**Oxazolidinone C**)

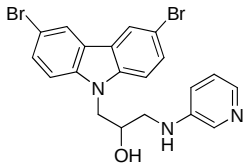


A mixture of oxazolidinone **A** (0.0390 g, 0.0920 mmol), 3-iodopyridine (0.0419 g, 0.204 mmol), CuI (0.0018 g, 0. 00920 mmol), and K_2CO_3 (0.0116 g, 0.0837 mmol) in 0.5 mL of DMSO was heated at 130 °C for 12 hours in a sealed vial. The reaction mixture was cooled and diluted with 20 mL EtOAc and washed with water 2×10 mL and brine 2×10 mL. The organic layer was dried over anhydrous Na_2SO_4 and evaporated to afford oxazolidinone **C** as a white solid (0.0383 g, 84%), which was used without further purification.

^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.44 (s, 1H), 8.37 (d, 1H, *J* = 4.2 Hz), 8.14 (d, 2H, *J* = 1.9 Hz), 8.03 (ddd, 1H, *J* = 1.2, 2.6, 8.5 Hz), 7.59 (dd, 2H, *J* = 1.9, 8.7 Hz), 7.34 (d, 2H, *J* = 8.7 Hz), 7.27 (dd, 1H, *J* = 4.9, 8.3 Hz), 5.15 (dt, 1H, *J* = 5.4, 11.8 Hz), 4.72–4.55 (m, 2H), 4.12 (dd, 1H, *J* = 7.9, 10.0 Hz), 3.82 (dd, 1H, *J* = 6.6, 9.1 Hz).

ESI *m/z* 543.9 ($[M + HCOO]^-$, $C_{22}H_{16}Br_2N_3O_4$ requires 544.0).

1-(3,6-Dibromo-9H-carbazol-9-yl)-3-(pyridin-3-ylamino)propan-2-ol (65)



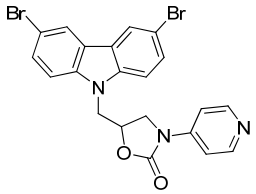
Following a procedure similar to that used to prepare **64**, **65** was prepared from oxazolidinone **C** in 79% yield.

^{1}H NMR ($CDCl_3$, 600 MHz) δ 8.11 (d, 2H, *J* = 1.6 Hz), 7.83 (br s, 2H), 7.52 (dd, 2H, *J* = 1.8, 8.7 Hz), 7.32 (d, 2H, *J* = 8.7 Hz), 7.02 (br s, 1H), 6.81 (d, 1H, *J* = 7.4 Hz), 4.45–4.33 (m, 3H), 3.30 (d, 1H, *J* = 11.8 Hz), 3.15 (dd, 1H, *J* = 6.2, 12.6 Hz).

^{13}C NMR ($CDCl_3$, 100 MHz) δ 139.8, 139.5, 136.2, 130.0, 129.5, 124.1, 123.8, 123.5, 119.7, 112.8, 110.9, 69.0, 47.6, 47.3.

ESI *m/z* 517.9 ([M + HCOO]$^-$, $C_{21}H_{18}Br_2N_3O_3$ requires 518.0).

5-((3,6-Dibromo-9H-carbazol-9-yl)methyl)-3-(pyridin-4-yl)oxazolidin-2-one (Oxazolidinone D)

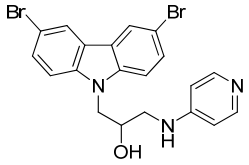


A mixture of oxazolidinone **A** (0.0195 g, 0.0460 mmol), 4-iodopyridine (0.0209 g, 0.102mmol), CuI (0.0009 g, 0. 00460 mmol), and K_2CO_3 (0.0058 g, 0.0418 mmol) in 0.5 mL of DMSO was at 130 °C for 12 h in a sealed vial. The reaction mixture was cooled and diluted with 20 mL EtOAc and washed with brine (3×10 mL). The organic layer was dried over anhydrous Na_2SO_4 and evaporated to afford the crude product, which was further triturated from a CH_2Cl_2 suspension by hexane to afford oxazolidinone D as a white solid (0.0187 g, 75)%.

^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.55 (br s, 2H), 8.16 (d, 2H, *J* = 1.8 Hz), 7.61 (dd, 2H, *J* = 1.8, 8.6 Hz), 7.37 (br s, 2H), 7.34 (d, 2H, *J* = 8.7 Hz), 5.23–5.10 (m, 1H), 4.64 (d, 2H, *J* = 4.6 Hz), 4.08 (t, 1H, *J* = 9.0 Hz), 3.77 (dd, 1H, *J* = 6.8, 9.4 Hz).

ESI *m/z* 544.0 ([M + HCOO]$^-$, $C_{22}H_{16}Br_2N_3O_4$ requires 544.0).

1-(3,6-Dibromo-9H-carbazol-9-yl)-3-(pyridin-4-ylamino)propan-2-ol (66)



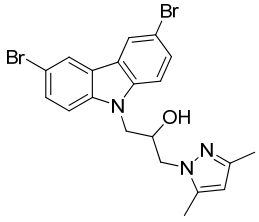
Following a procedure similar to that used to prepare **64**, **66** was prepared from oxazolidinone **D** in 7% yield (reaction time was shortened to 3 d).

^{1}H NMR (acetone-d_6, 400 MHz) δ 8.37 (s, 2H), 8.10 (br s, 2H), 7.62 (d, 2H, *J* = 8.7 Hz), 7.56 (d, 2H, *J* = 8.6 Hz), 6.61 (s, 2H), 4.61 (dd, 1H, *J* = 3.4, 14.8 Hz), 4.51 (dd, 1H, *J* = 7.6, 15.0 Hz), 4.41 (dt, 1H, *J* = 4.1, 7.6 Hz), 3.49 (dd, 1H, *J* = 4.4, 13.2 Hz), 3.33 (dd, 1H, *J* = 6.4, 13.1 Hz).

^{13}C NMR (acetone-d_6, 100 MHz) δ 179.0, 149.6, 140.4, 129.0, 123.8, 123.3, 112.1, 111.8, 107.8, 68.8, 47.6, 46.4.

ESI *m/z* 517.9 ([M + HCOO]$^-$, $C_{21}H_{18}Br_2N_3O_3$ requires 518.0).

1-(3,6-Dibromo-9H-carbazol-9-yl)-3-(3,5-dimethyl-1H-pyrazol-1-yl)propan-2-ol (67)



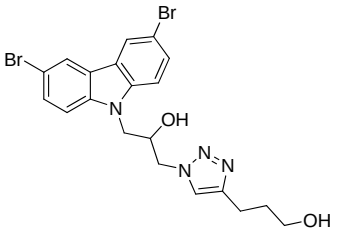
Following a literature procedure[18], **30** (56 mg, 0.136 mmol) was added to a 25 mL scintillation vial, followed by the addition of acetylacetone (13.7 mg, 0.136 mmol) in 1 mL of EtOH and heated to 70 °C for 1 h. Upon completion the reaction was cooled to room temperature and concentrated under reduced pressure. The crude residue was purified by chromatography (SiO_2, 0–50% EtOAc/Hexane) to afford **67** as an off-white solid (29 mg, 45%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.12 (d, 2H, *J* = 1.9 Hz), 7.51 (dd, 2H, *J* = 1.9, 8.7 Hz), 7.14 (d, 2H, *J* = 8.7 Hz), 5.79 (s, 1H), 5.19–5.10 (br s, 1H), 4.51 (m, 1H), 4.38 (s, 1H), 4.36 (s, 1H), 3.92 (dd, 1H, *J* = 3.0, 13.8 Hz), 3.69 (dd, 1H, *J* = 6.4, 13.8 Hz), 2.21 (s, 3H), 1.85 (s, 3H).

^{13}C NMR ($CDCl_3$, 100 MHz) δ 148.4, 140.3, 139.6 (2C), 129.4 (2C), 123.8 (2C), 123.4 (2C), 112.7 (2C), 110.9 (2C), 105.3, 69.7, 49.9, 46.5, 13.7, 11.0.

ESI *m/z* 475.9 $([M+H])^+$, $C_{20}H_{20}Br_2N_3O$ requires 476.0).

3-(1-(3-(3,6-Dibromo-9H-carbazol-9-yl)-2-hydroxypropyl)-1H-1,2,3-triazol-4-yl)propan-1-ol (68)



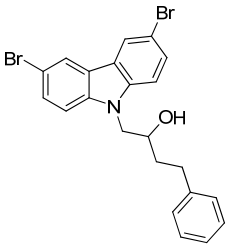
Following a literature procedure[19], **31** (111 mg, 0.262 mmol) and 4-pentyne-1ol (44 mg, 0.5 mmol) were suspended in 1 mL of a 3:1 water/*t*-BuOH mixture. Sodium ascorbate (10 mg, 0.052 mmol) was added followed by $CuSO_4 \bullet H_2O$ (2 mg, 0.01 mmol). The heterogeneous mixture was stirred at room temperature for 12 h. Upon completion, the reaction was partitioned between EtOAc and H_2O. The aqueous layer was washed 3×EtOAc. The organic extract was combined and washed with brine, dried over Na_2SO_4, filtered, and concentrated in vacuo. The crude residue was purified by chromatography (SiO_2, 0–0% EtOAc/Hexane) to afford **68** as an off-white solid (72 mg, 54%).

^{1}H NMR (d_6-DMSO, 400 MHz) δ 8.47 (d, 2H, *J* = 1.1 Hz), 7.82 (s, 1H), 7.61 (m, 4H), 5.46 (d, 1H, *J* = 5.6 Hz), 4.55 (dd, 1H, *J* = 3.3, 13.7 Hz), 4.5–4.42 (m, 2H), 4.42–4.24 (m, 3H), 3.43 (dd, 2H, *J* = 6.3, 11.6 Hz), 2.64 (t, 2H, *J* = 7.6 Hz), 1.79–1.64 (m, 2H).

^{13}C NMR (acetone-d_6, 125 MHz) δ 148.0, 141.1, 129.8, 124.6, 124.1, 123.4, 112.8, 112.7, 70.2, 70.1, 54.3, 48.0, 33.5, 22.9.

ESI *m/z* 506.9 $([M+H]^+$, $C_{20}H_{21}Br_2N_4O_2$ requires 507.0).

1-(3,6-Dibromo-9H-carbazol-9-yl)-4-phenylbutan-2-ol (69)



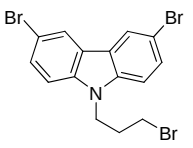
3,6-Dibromocarbazole (100 mg, 0.307 mmol) was treated with KOH (21 mg, 0.369 mmol, freshly ground) in 1 mL DMF for 1 h at room temperature. 2-Phenethyloxirane (55 mg, 0.369 mmol) in 500 µL of DMF was added and reaction was stirred overnight at 60 °C[ii]. Upon completion, the reaction was cooled to room temperature and poured over ice. The aqueous layer was washed 3×EtOAc. The organic extracts were combined and washed with brine, dried over Na_2SO_4, filtered, and concentrated in vacuo. The crude residue was purified by chromatography (SiO_2, 0–50% EtOAc/Hexane) to afford **69** as an off-white solid (102 mg, 70%).

^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.12 (d, 2H, *J* = 1.9 Hz), 7.52 (dd, 2H, *J* = 1.9, 8.7 Hz), 7.32–7.24 (m, 2H), 7.23–7.15 (m, 3H), 4.27–4.20 (m, 2H), 4.17–4.05 (m, 1H), 2.94–2.81 (m, 1H), 2.80–2.66 (m, 1H), 1.93 (dd, 2H, *J* = 7.9, 13.9 Hz), 1.64 (d, 1H, *J* = 4.3 Hz).

^{13}C NMR ($CDCl_3$, 100 MHz) δ 141.2, 139.9 (2C), 129.4 (2C), 128.8 (2C), 128.6 (2C), 126.4 (2C), 123.7, 123.4 (2C), 112.6 (2C), 111.0 (2C), 70.4, 50.1, 36.4, 32.0.

ESI *m/z* 471.9 $([M+H])^+$, $C_{22}H_{20}Br_2NO$ requires 472.0).

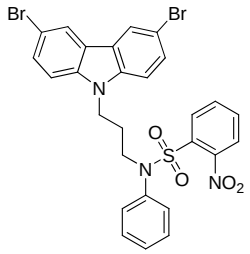
3,6-Dibromo-9-(3-bromopropyl)-9H-carbazole (Bromopropane A)



Crushed KOH (0.0673 g, 1.20 mmol, 1.2 equiv) was added to 3,6-dibromocarbazole (0.3250 g, 1.00 mmol) in 2 mL DMF solution and the mixture was stirred for 30 min. 1,3-Dibromopropane (0.5047 g, 2.50 mmol, 2.5 equiv) in 3 mL DMF solution was added dropwise into the mixture and it was stirred at room temperature overnight. The crude reaction mixture was diluted with 30 mL EtOAc and washed with 2×10 mL 1M HCl and with 3×10 mL water. The organic layer was dried over anhydrous Na_2SO_4 and evaporated to afford the crude product, which was purified by chromatography (SiO_2, Hexanes/EtOAc) to afford bromopropane **A** as a colorless oil (0.1275 g, 29%).

^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.02 (d, 2H, *J* = 1.7 Hz), 7.51 (dd, 2H, *J* = 2.0, 8.7 Hz), 7.26 (d, 2H, *J* = 8.8 Hz), 4.33 (t, 2H, *J* = 6.6 Hz), 3.29 (t, 2H, *J* = 6.1 Hz), 2.24–2.44 (m, 2H).

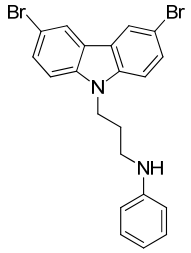
***N*-(3-(3,6-Dibromo-9H-carbazol-9-yl)propyl)-2-nitro-*N*-phenylbenzenesulfonamide (Ns-I)**



Following a modified literature procedure[20], crushed KOH (0.0024 g, 0.0431 mmol) was added to 2-nitro-*N*-phenylbenzenesulfonamide (0.0100 g, 0.0359 mmol) in 0.2 mL DMF solution and the mixture was stirred for 30 min. Bromopropane **A** (0.0240 g, 0.0538 mmol) in 0.3 mL DMF solution was added dropwise into the mixture and it was stirred at room temperature overnight. The crude reaction mixture was diluted with 20 mL EtOAc and washed with 5×10 mL water. The organic layer was dried over anhydrous Na_2SO_4 and evaporated to afford the crude product, which was purified by chromatography (SiO_2, Hexanes/EtOAc) to afford Ns-**I** as an impure white solid (0.0082 g, purity 66.9%; impurity is starting Ns-aniline; used without additional purification, 36% yield).

^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.09 (d, 2H, *J* = 1.9 Hz), 7.59–7.71 (m, 2H), 7.51 (dd, 2H, *J* = 2.0, 8.7 Hz), 7.41–7.44 (m, 2H), 7.32 (d, 2H, *J* = 3.7 Hz), 7.18–7.25 (m, 3H), 7.17 (s, 1H), 7.15 (s, 1H), 4.32–4.38 (m, 2H), 3.95 (t, 2H, *J* = 6.6 Hz), 1.89–2.01 (m, 2H).

***N*-(3-(3,6-Dibromo-9H-carbazol-9-yl)propyl)aniline (70)**



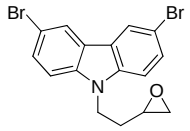
Ns-**I** (0.0378 g, 0.0588 mmol, 1 equiv), cesium carbonate (0.057 4 g, 0.176 mmol, 3 equiv) and benzenethiol (0.0194 g, 0.176 mmol) were mixed in 1 mL anhydrous THF. The mixture was stirred at room temperature for 3 h. THF was removed under vacuum and the residue was purified by chromatography (SiO_2, Hexanes/EtOAc) to afford **70** as a colorless oil (0.0164 g, 61%).

^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.12 (d, 2H, *J* = 1.9 Hz), 7.51 (dd, 2H, *J* =2.0, 8.7 Hz), 7.25 (d, 2H, *J* = 8.7 Hz), 7.16 (dd, 2H, *J* = 7.4, 8.5 Hz), 6.73 (t, 1H, *J* = 7.3 Hz), 6.53 (dd, 2H, *J* = 1.0, 8.6 Hz), 4.37 (t, 2H, *J* = 6.7 Hz), 3.55 (br s, 1H), 3.09 (t, 2H, *J* = 6.6 Hz), 2.08–2.29 (m, 2H).

^{13}C NMR ($CDCl_3$, 100 MHz) δ 148.0, 139.5, 129.6, 129.4, 123.7, 123.6, 118.2, 113.3, 112.4, 110.5, 41.4, 40.9, 28.9.

ESI *m/z* 456.9 ($[M+H]^+$ $C_{21}H_{19}Br_2N_2$ requires 457.0).

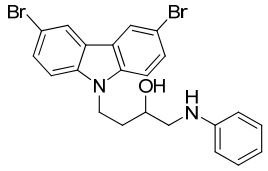
3,6-Dibromo-9-(2-(oxiran-2-yl)ethyl)-9H-carbazole (Epoxide L)



Crushed KOH (0.0054 g, 0.0954 mmol, 1.2 equiv) was added to 3,6-dibromocarbazole (0.0258 g, 0.0795 mmol, 1equiv) in 0.5 mL DMF solution and the mixture was stirred for 30 min. 1-Bromo-3,4-epoxybutane (0.0300 g, 0.199 mmol) in 0.5 mL DMF solution was added dropwise into the mixture and it was stirred at room temperature for overnight. The crude reaction was diluted with 20 mL EtOAc and washed with 5×10 mL water. The organic layer was dried over anhydrous Na_2SO_4 and evaporated to afford epoxide **L** as a white solid (31.2 mg, 98%).

^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.08 (d, 2H, *J* = 1.9 Hz), 7.50 (dd, 2H, *J* = 1.9, 8.7 Hz), 7.27 (d, 2H, *J* = 8.7 Hz), 4.26–4.54 (m, 2H), 2.69–2.80 (m, 1H), 2.64 (dd, 1H, *J* = 4.1, 4.8 Hz), 2.34 (dd, 1H, *J* = 2.6, 4.9 Hz), 2.13–2.27 (m, 1H), 1.65–1.81 (m, 1H).

4-(3,6-Dibromo-9H-carbazol-9-yl)-1-(phenylamino)butan-2-ol (71)



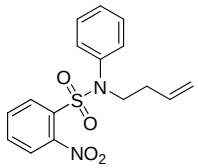
According to Representative Procedure 2 using $BiCl_3$, **71** was prepared from epoxide **L** to afford a white solid in 31% yield.

^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.14 (d, 2H, *J* = 1.9 Hz), 7.60 (dd, 2H, *J* = 1.9, 8.7 Hz), 7.38 (d, 2H, *J* = 8.7 Hz), 7.15 (dd, 2H, *J* = 7.6, 8.3 Hz), 6.74 (t, 1H, *J* = 7.3 Hz), 6.57 (d, 2H, *J* = 7.7 Hz), 4.51–4.60 (m, 1H), 4.39–4.48 (m, 1H), 3.60–3.74 (m, 1H), 3.09–3.17 (dd, 1H, *J* = 8.3, 13.2 Hz), 2.99–3.07 (dd, 1H, *J* = 3.4, 13.2 Hz), 2.05–2.14 (m, 1H), 1.87 –1.98 (m, 1H).

^{13}C NMR ($CDCl_3$, 125 MHz) δ 148.1, 139.6, 129.6, 129.4, 123.8, 123.6, 118.7, 113.6, 112.4, 110.8, 67.7, 51.0, 39.9, 33.7.

ESI *m/z* 486.9 ($[M+H]^+$ for $C_{22}H_{21}Br_2N_2O$ requires 487.0).

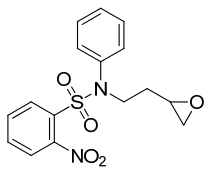
***N*-(But-3-enyl)-2-nitro-*N*-phenylbenzenesulfonamide (Ns-J)**



Crushed KOH (0.0484 g, 0.862 mmol, 1.2 equiv) was added to 2-nitro-*N*-phenylbenzenesulfonamide (0.200 g, 0.719 mmol) in 1 mL DMF, and the mixture was stirred for 30 min. 4-Bromo-1-butene (0.2426 g, 1.80 mmol) in 2 mL DMF solution was added dropwise into the mixture and it was stirred at room temperature overnight. The reaction mixture was diluted with 30 mL EtOAc and washed with 2×10 mL 1M HCl and 3×10 mL water. The organic layer was dried over anhydrous Na_2SO_4 and evaporated to afford the crude product, which was purified via chromatography (SiO_2, Hexanes/EtOAc) to afford Ns-**J** as a white solid (0.1546 g, 64%).

^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.60–7.66 (m, 1H), 7.52–7.58 (m, 1H), 7.42–7.46 (m, 2H), 7.30 (d, 2H, *J* = 1.9 Hz), 7.14–7.21 (m, 3H), 5.64–5.83 (m, 1H), 5.03 (s, 1H), 5.00 (d, 1H, *J* = 4.4 Hz), 3.83 (t, 2H, *J* = 7.2 Hz), 2.20 (q, 2H, *J* = 6.9 Hz).

2-Nitro-*N*-(2-(oxiran-2-yl)ethyl)-*N*-phenylbenzenesulfonamide (Epoxide M)

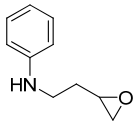


m-CPBA (77%, 0.0550 g, 0.246 mmol) was added to Ns-**J** (0.0653 g, 0.196 mmol) in 1 mL $CHCl_3$ at 0 °C. The mixture was stirred at 0 °C for 30 min, then gradually warmed up to room temperature and continued to stir for 18 h. After TLC showed the disappearance of starting material, the reaction mixture was diluted with a 1:1 mixture of water and saturated $NaHCO_3$ (2×10 mL) and water (10 mL). The organic layer was dried over anhydrous Na_2SO_4 and evaporated to afford the crude product, which was purified by chromatography (SiO_2, Hexanes/EtOAc) to afford epoxide **M** as a colorless oil (0.0662 g, 97%).

^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.57–7.66 (m, 2H), 7.43–7.47 (m, 2H), 7.28–7.34 (m, 3H), 7.19–7.23 (m, 2H), 3.87–4.07 (m, 2H), 2.93–3.03 (m, 1H), 2.70–2.80 (m, 1H), 2.46 (dd, 1H, *J* = 2.7, 5.0 Hz), 1.66–1.79 (m, 2H).

ESI *m/z* 371.0 ($[M+Na]^+$ for $C_{16}H_{16}N_2NaO_5S$ requires 371.1).

_N_-(2-(Oxiran-2-yl)ethyl)aniline (Epoxide N)

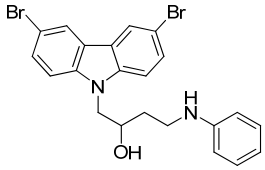


Prepared from epoxide **M** using a procedure analogous to that used to prepare **70**.

^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.18 (dd, 2H, *J* = 7.4, 8.5 Hz), 6.71 (t, 1H, *J* = 7.3 Hz), 6.62 (d, 2H, *J* = 7.7 Hz), 3.87 (br s, 1H), 3.31 (t, 2H, *J* = 6.6 Hz), 3.00–3.10 (m, 1H), 2.79 (t, 1H, *J* = 4.4 Hz), 2.55 (dd, 1H, *J* = 2.7, 4.9 Hz), 1.98–2.15 (m, 1H), 1.64–1.79 (m, 1H).

ESI *m/z* 164.1 ($[M+H]^+$ for $C_{10}H_{14}NO$ requires 164.1).

1-(3,6-Dibromo-9H-carbazol-9-yl)-4-(phenylamino)butan-2-ol (72)



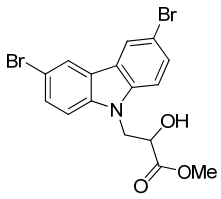
NaH (60% dispersion in mineral oil, 0.0018 g, 0.0452 mmol) was added to a solution of 3,6-dibromocarbazole (0.0147 g, 0.0452 mmol) in 0.5 mL anhydrous THF and the mixture was stirred for 15 min. Epoxide **N** (0.0067 g, 0.0410 mmol) in 1.5 mL anhydrous THF solution was added dropwise and the resulting mixture was stirred at 60 °C overnight. THF was removed under vacuum and the residue was dissolved in 10 mL EtOAc and washed with water 2×5 mL. The organic layer was dried over anhydrous Na_2SO_4 and evaporated to afford the crude product, which was purified by chromatography (SiO_2, Hexanes/EtOAc) to afford **72** as a colorless oil (0.0115 g, 58%).

^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.12 (d, 2H, *J* = 2.0 Hz), 7.54 (dd, 2H, *J* = 2.0, 8.7 Hz), 7.31 (d, 2H, *J* = 8.7 Hz), 7.18 (t, 2H, *J* = 8.0 Hz), 6.76 (t, 1H, *J* = 7.3 Hz), 6.63 (d, 2H, *J* = 8.5 Hz), 4.20–4.38 (m, 3H), 3.22–3.41 (m, 2H), 1.76–1.95 (m, 2H).

^{13}C NMR ($CDCl_3$, 100 MHz) δ 148.1, 139.9, 129.6, 129.5, 123.8, 123.5, 118.7, 113.9, 112.7, 111.1, 70.7, 50.0, 42.2, 34.1.

ESI *m/z* 531.0 ($[M + HCOO]^-$, $C_{23}H_{21}Br_2N_2O_3$ requires 531.0); 486.9 ($[M+H]^+$ for $C_{22}H_{21}Br_2N_2O$ requires 487.0).

Methyl 3-(3,6-Dibromo-9H-carbazol-9-yl)-2-hydroxypropanoate (Ester A)



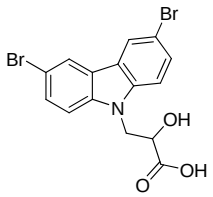
3,6-Dibromocarbazole (0.300 g, 0.923 mmol) was dissolved in DMF (1.2 mL) and cooled to 0 °C. NaH (60% dispersion in mineral oil, 0.074 g, 1.846 mmol) was added and the reaction stirred for 1 h at 0 °C. Methyl glycidate (0.471 g, 4.615 mmol) was added and the reaction was stirred and warmed to ambient temperature over 3.5 h. Upon completion by TLC the reaction mixture was partitioned between EtOAc and H_2O. The aqueous layer was extracted 3×EtOAc, and the combined organics were washed with saturated aqueous NaCl, dried

over Na_2SO_4, filtered, and concentrated in vacuo. The crude residue was purified by chromatography (SiO_2, 0–30% EtOAc/Hexane) to afford ester **A** (125 mg, 32%).

^{1}H NMR ($CDCl_3$, 500 MHz) δ 8.10 (d, 2H, *J* = 2.0 Hz), 7.53 (dd, 2H, *J* = 2.0, 9.0 Hz), 7.36 (d, 2H, *J* = 9.0 Hz), 4.63–4.55 (m, 3H), 3.69 (s, 3H), 2.94 (d, 1H, *J* = 5.5 Hz).

ESI *m/z* 425.8 ($[M+H]^+$, $C_{16}H_{14}Br_2NO_3$ requires 425.9).

3-(3,6-Dibromo-9H-carbazol-9-yl)-2-hydroxypropanoic acid (Acid A)

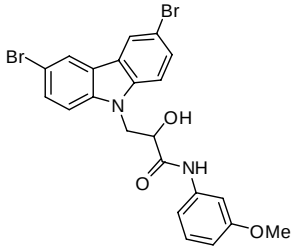


NaOH (0.64 mL, 1M solution in H_2O) was added to a suspension of ester **A** (0.055 g, 0.129 mmol) in EtOH (2.6 mL) and the reaction was stirred at ambient temperature for 2.5 h. The reaction was concentrated in vacuo and the residue was acidified with 1N aqueous HCl. The mixture was extracted 3×EtOAc and the combined organics were washed with saturated aqueous NaCl, dried over Na_2SO_4, filtered, and concentrated in vacuo to afford acid **A** as a white solid (53 mg, 99%).

^{1}H NMR ($CDCl_3$, 500 MHz) δ 8.10 (d, 2H, *J* = 1.5 Hz), 7.52 (dd, 2H, *J* = 1.5, 8.5 Hz), 7.40 (d, 2H, *J* = 9.0 Hz), 4.68 (m, 2H), 4.60 (dd, 1H, *J* = 6.5, 15.5 Hz).

ESI *m/z* 411.9 ($[M+H]^+$, $C_{15}H_{12}Br_2NO_3$ requires 411.9).

3-(3,6-Dibromo-9H-carbazol-9-yl)-2-hydroxy-*N*-(3-methoxyphenyl)propanamide (73)

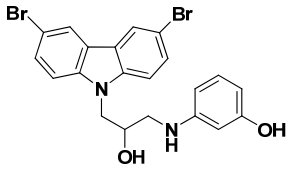


Acid **A** (0.025 g, 0.061 mmol) was suspended in anhydrous CH_2Cl_2 and cooled to 0 °C. Thionyl chloride (0.005 mL, 0.073 mmol) was added dropwise and the reaction was stirred at 0 °C for 1 h. *m*-Anisidine (0.008 mL, 0.073 mmol) and Et_3N (0.010 mL, 0.073 mmol) were added and the reaction was allowed to warm to ambient temperature over 2.5 h. Upon completion, the solution was partitioned between EtOAc and H_2O. The aqueous layer was washed 3×EtOAc, and the combined organics were washed with saturated aqueous NaCl, dried over Na_2SO_4, filtered, and concentrated in vacuo. The crude residue was purified by chromatography (SiO_2, 0–30% EtOAc/Hexane) to afford **73** (15 mg, 48%).

^{1}H NMR (acetone-d_6, 500 MHz) δ 9.22 (br s, 1H), 8.34 (d, 2H, *J* = 1.5 Hz), 7.65 (d, 2H, *J* = 8.5 Hz), 7.59 (dd, 2H, *J* = 4.0, 8.5 Hz), 7.42 (dd, 1H, *J* = 2.0 Hz), 7.24 (m, 1H), 7.20 (dd, 1H, *J* = 8.0 Hz), 6.67 (dd, 1H, *J* = 2.0, 8.0 Hz), 5.56 (br s, 1H), 4.82 (m, 1H), 4.73 (m, 2H), 3.77 (s, 3H).

^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.9, 161.1, 141.1, 140.3, 130.3 (2C), 129.8 (2C), 124.6 (2C), 124.0 (2C), 113.1 (2C), 112.8 (2C), 112.7, 110.5, 106.4, 72.7, 55.6, 48.4.

ESI *m/z* 514.9 ($[M–H]^-$, $C_{22}H_{17}Br_2N_2O_3$ requires 515.0).

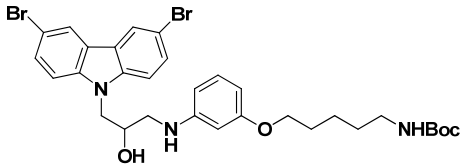


3-(3-(3,6-dibromo-9H-carbazol-9-yl)-2-hydroxypropylamino)phenol (74)

Boron tribomide (0.28 ml, 3.0 mmol) was added to a solution of **7** (100.6 mg, 0.20 mmol) in anhydrous dichloromethane (1.6 ml, 0.12 M) in a in an ice bath. The cold bath was removed after 5 minutes, and the reaction mixture was stirred until starting material was consumed as judged by LC/MS. The reaction was quenched with saturated $NaHCO_3$. The mixture was diluted with EtOAc, washed twice with water and then brine. The organic layer was dried over Na_2SO_4, filtered and condensed. Flash chromatography on silica gel provided the purified product (2% MeOH/DCM). Yield=74%

^{1}H NMR ($CDCl_3$, 400 MHz) 8.10 (s, 2H), 7.51 (d, 2H, *J* = 8.8 Hz), 7.26 (m, 2H), 6.99 (t, 1H, *J* = 8.1 Hz), 6.21 (d, 1H, *J* = 8.4 Hz), 6.16 (d, 1H, *J* = 8.4 Hz), 6.04 (s, 1H), 5.31 (s, 1H), 4.29 (m, 3H), 3.05-3.27 (m, 2H).

MS (ESI), m/z: calculated 487.97, found 532.7 $(M+HCOO)^-$.

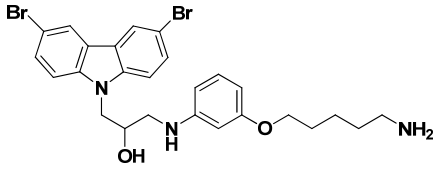


tert-butyl 5-(3-(3-(3,6-dibromo-9H-carbazol-9-yl)-2-hydroxypropylamino)phenoxy)pentylcarbamate (75)

A solution phenol **74** (72.2 mg, 0.15 mmol), 5-(tert-butoxycarbonylamino)pentyl methanesulfonate (133.7 mg, 0.48 mmol) and potassium carbonate (65.3 mg, 0.47 mmol) in DMF (2.0 ml) in a scintillation vial was heated at 90 ^{0}C overnight, after which all SM had been consumed. The reaction mixture was cooled and diluted with EtOAc and washed several times with water and then brine. The organic layer was dried over Na_2SO_4, filtered and condensed. Flash chromatography on silica gel (40% EtOAc/hexanes) provided the purified product. Yield=73%

^{1}H NMR ($CDCl_3$, 500 MHz) 8.14 (d, 2H, *J* = 1.6 Hz), 7.54 (dd, 2H, *J* = 8.7, 1.7 Hz), 7.35 (d, 2H, *J* = 8.7 Hz), 7.07 d, 1H, *J* = 7.8 Hz), 6.30 (dd, 1H, *J* = 8.2, 2.1 Hz), 6.22 (dd, 1H, *J* = 8.4, 1.8 Hz), 4.55 (bs, 1H), 4.34-4.46 (m, 3H), 3.86 (t, 2H, *J* = 6.3 Hz), 3.10-3.35 (m, 4H), 2.90 (s, 1H), 2.43 (bs, 1H), 1.76 (m, 2H), 1.46-1.58 (m, 4H), 1.44 (s, 9H).

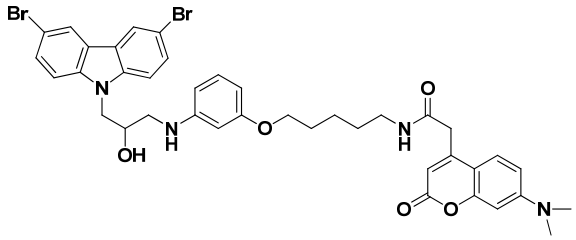
MS (ESI), m/z: calculated 673.12, found 674.1 $(M+1)^+$.



1-(3-(5-aminopentyloxy)phenylamino)-3-(3,6-dibromo-9H-carbazol-9-yl)propan-2-ol (amine A)

Trifluoroacetic acid (50 μl, 0.649 mmol) was added dropwise to a solution of carbamate **75** (25.0 mg, 0.037 mmol) in dichloromethane (2.0 ml). Once all the starting material had been consumed the reaction was condensed and the crude reaction product was used without purification.

MS (ESI), m/z: calculated 573.06, found 574.0 $(M+1)^+$.



N-(5-(3-(3-(3,6-dibromo-9H-carbazol-9-yl)-2-hydroxypropylamino)phenoxy)pentyl)-2-(7-(dimethylamino)-2-oxo-2H-chromen-4-yl)acetamide

A solution of 2-(7-(dimethylamino)-2-oxo-2H-chromen-4-yl)acetic acid (2.5 mg, 0.0092 mmol) and EDC (2.4 mg, 0.013 mmol) in 0.3 ml DMF was cooled in an ice bath before the addition of a solution of amine **A** (5.3 mg, 0.0092 mmol) in 0.2ml DMF. An additional 0.4 ml DMF was introduced to the reaction vial. Hunig's base (10 μl, 0.057 mmol) was added to the cold solution which was then slowly warmed to ambient temperature. After 12 h, additional acid (3.3 mg, 0.013 mmol) was treated with EDC (2.6 mg, 0.013 mmol) in 0.2 ml cold DMF and then added to the reaction mixture. After an additional 24 h, the reaction mixture was diluted with EtOAc, and washed several times with water and then brine. The organic layer was dried over Na_2SO_4, filtered and condensed. Preparative TLC provided the purified product (5%MeOH/DCM); 1.9 mg isolated, yield=26%.

^{1}H NMR ($(CD_3)_2CO$), 400 MHz) □ 8.36 (d, 2H, *J* = 1.7 Hz), 7.52-7.63 (m, 4H), 6.97 (t, 1H, *J* = 8.0 Hz), 6.66 (dd, 1H, *J* = 8.9, 2.5 Hz), 6.26 (dd, 1H, J=7.8, 1.4 Hz), 6.22 (m, 1H), 6.17 (dd, 1H, *J* = 8.1, 2.1 Hz), 6.02 (bs, 1H), 5.10 (m, 1H), 4.43-4.64 (m, 2H),4.37 (m, 1H), 3.81 (t, 2H, *J* = 6.3 Hz), 3.63 (s, 2H), 3.19-3.41 (m, 4H), 3.03 (s, 6H), 1.69 (m, 2H), 1.53 (m, 2H), 1.41 (m, 2H).

MS (ESI), m/z: calculated 802.14, found 803.1 $(M+1)^+$.

1 Asso, V.; Ghilardi, E.; Bertini, S.; Digiacomo, M.; Granchi, C.; Minutolo, F.; Rapposelli, S.; Bortolato, A.; Moro, S. Macchia, M. *ChemMedChem*, **2008**, *3*, 1530.

2 Fukuyama, T.; Jow, C.-K.; Cheung, M. *Tetrahedron Lett*. **1995**, *36*, 6373.

3 Beyer, M.; Fritscher, J.; Feresin, E.; Schiemann, O. *J. Org. Chem*. **2003**, *68*, 2209.

4 Zhu, W.; Ma, D. *Chem. Comm*. **2004**, 888.

5 Chemistry of Heterocyclic Compounds volume 41, No 4, 2005, pg 426.

6 Weissman, S. A.; Zewge, D.; Chen, C. *J. Org. Chem*. **2005**, *70*, 1508.

7 Maegawa, Y.; Goto, Y.; Inagaki, S.; Shimada, T. *Tetrahedron Letters*, **2006**, *47*, 6957.

8 Gundersen, E. G. U.S. Patent App. Publ. (**2005**) US 2005070592 AI 20050331.

9 Guangyou, Z.; Yuquing, L.; Zhaohui, W.; Nohira, H.; Hirose, T. *Tetrahedron: Asymmetry*, **2003**, *14*, 3297.

10 Ravlee, I.; Sivakumar, R.; Muruganantham, N.; Anbalagan, N.; Gunasekaran, V.; Leonard, J. T. *Chem. Pharm. Bull.* **2003**, *51*, 162.

11 Manetti, F.; Santucci, A.; Locatelli, G. A.; Maga, G.; Spreafico, A.; Serchi, T.; Orlandini, M.; Bernardini, G.; Caradonna, N. P.; Spallarossa, A.; Brullo, C.; Schenone, S.; Bruno, O.; Ranise, A.; Bondavalli, F.; Hoffmann, O.; Bologna, M.; Angelucci, A.; Botta, M. *J. Med. Chem.* **2007**, *50*, 5579.

12 Harbert, C. A.; Plattner, J. J.; Welch, W. M.; Weissman, A.; Koe, B. K. *J. Med. Chem*. **1980**, *23*, 635.

13 Chakraborti, A. K.; Rudrawar, S.; Kondaskar, A. *Eur. J. Org. Chem*. **2004**, 3597.

14 Ludwig, J.; Bovens, S.; Brauch, C.; Elfringhoff, A. S.; Lehr, M. *J. Med. Chem.* **2006**, *49*, 2611.

15 Ponce, M. A.; Erra-Balsells, R. *J. Heterocyclic Chem*. **2001**, *38*, 1087.

16 Morcuende, A.; Ors, M.; Valverde, S.; Herradón, B. *J. Org. Chem.* **1996**, *61*, 5264.

17 Tatsumi, R.; Fujio, M.; Satoh, H.; Katayama, J.; Takanashi, S.; Hashimoto, K.; Tanaka, H. et al. *J. Med. Chem*. **2005**, *48*, 2678.

18 Kolb, H. C.; Finn, M. G.; Sharpless, K. B. *Angew. Chem. Int. Ed.* **2001**, *40*, 2004.

19 Cosyn, L.; Palaniappan, K. K.; Kim, S.–K.; Duong, H. T.; Gao, Z.–G.; Jacobson, K. A.; Van Calenbergh, S. *J. Med. Chem*. **2006**, *49*, 7373.

20 Basle, E.; Jean, M.; Gouault, N.; Renault, J.; Uriac, P. *Tetrahedron Letters* **2007**, *48*, 8138.